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# STERNAL MARROW PUNCTURE IN INFANTS AND IN CHILDREN

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Biopsy of superficially lying tissues, such as the skin, the muscle and the subcutaneous lymph nodes, has long been a common diagnostic procedure in cases of obscure conditions in which routine clinical and laboratory examinations offer little or no definite information. Though not a new procedure, biopsy of the bone marrow in cases of various types of blood dyscrasia has only recently become popular as a diagnostic measure, largely because of the simplification of the technic and the growing conviction on the part of many observers that in certain instances the peripheral blood reflects only meagerly the more acute pathologic changes in the marrow. Modern research workers in hematology have come more and more to emphasize the two distinct physiologic processes involved in the normal maintenance of cellular balance in the blood, namely, (1) the normal maturation of various blood cells in the hematopoietic centers and (2) the normal rate of delivery of mature elements into the general circulation. When these two factors function in their normal relationship, the peripheral blood as well as the hematopoietic organs are said to be in a state of physiologic equilibrium. Therefore, knowledge of the actual nature and condition of the marrow is exceedingly valuable in establishing the final diagnosis of the disease, especially when the peripheral blood reveals no convincing proof of the suspected pathologic condition.

## HISTORY AND LITERATURE OF STERNAL BIOPSY

The earliest experience with biopsy of the bone marrow was recorded by Wolff,[1] who undertook diaphysial trepanation of the tibias of small animals in the laboratory. This method was first applied in

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From the Department of Pediatrics and the Bobs Roberts Memorial Hospital for Children, the University of Chicago.

1. Wolff, A.: Ueber eine Methode zur Untersuchung des lebenden Knochenmarks von Thieren und über das Bewegungsvermögen der Myelocyten, Deutsche med. Wchnschr. **20**:165, 1903.

the study of human subjects by Ghedini,[2] who selected patients with latent malaria or leishmaniasis and observed that the parasites were present in the bone marrow but absent from the peripheral blood. Ghedini's technic utilized a small bone trephine, and the tibial marrow was the tissue usually removed for his studies, a method which has ever since remained a useful and practical procedure for biopsy of the bone marrow of human subjects. Many subsequent workers, among them Spuler and Schittenhelm,[3] Caronia,[4] Kramar and Hensch [5] and Peabody,[6] used this technic and published their observations on the marrow picture in various diseases. From time to time modifications of the original technic have been presented, such as those by Morris and Falconer,[7] Tuohy and Gillespie [8] and others.

One important consideration in the biopsy of bone marrow is the selection of the marrow from which the sample tissue is to be obtained. The tibial marrow is active from birth until about the age of 7 years, at which time fatty metamorphosis gradually turns it yellow so that by the age of 15 it is almost completely inactive, as noted by Neumann,[9] Hedinger,[10] Piney,[11] Askanazy [12] and Turnbull.[13] Thus, except in diseases causing definite changes in the fatty marrow (notably pernicious

2. Ghedini, G.: Per la patogenesi e per la diagnosi delle malattie del sangue e degli organi emopoietici, punctura esplorativa del midollo osseo, Clin. med. ital. **47**:724, 1908.

3. Spuler, A., and Schittenhelm, A.: Ueber die Herkunft der sogenannten "Kern" r. "Zellschollen" bei lymphatischer Leukämie und die Natur der eosinophilen Zellen zugleich ein Beitrag zur diagnostischen Knochenmarkspunktion, Deutsches Arch. f. klin. Med. **109**:1, 1912.

4. Caronia, G.: La punctura della milza e del midollo osseo, Pediatria **30**: 607, 1922.

5. Kramar, E., and Hensch, V.: Knochenmarkuntersuchungen bei Säuglingen, Monatschr. f. Kinderh. **30**:440, 1925.

6. Peabody, F. W.: The Pathology of the Bone Marrow in Pernicious Anemia, Am. J. Path. **3**:179, 1927.

7. Morris, L. M., and Falconer, E. H.: Intravitam Bone Marrow Studies; Preliminary Report: I. Description of a Marrow Trephine and Experimental Studies, Arch. Int. Med. **30**:485 (Oct.) 1922; II. Survey of Clinical Fields, ibid. **30**:490 (Oct.) 1922.

8. Tuohy, E. L., and Gillespie, M. G.: A Trephine Modified to Secure Bone Marrow (Sternal) Biopsies, J. A. M. A. **104**:1404 (April 20) 1935.

9. Neumann, E.: Das Gesetz der Verbreitung des roten und gelben Knochenmarkes, Centralbl. f. d. med. Wissensch. **30**:321, 1882.

10. Hedinger, E.: Die Verbreitung des roten Knochenmarks im Oberschenkel des Menschen, Berl. klin. Wchnschr. **50**:2121, 1913.

11. Piney, A.: The Anatomy of the Bone Marrow, Brit. M. J. **2**:792 (Oct. 28) 1922.

12. Askanazy, M.: Knochenmark, in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie, Berlin, Julius Springer, 1927, vol. 1, pt. 2.

13. Turnbull, H. M., in Vaughan, J. M.: The Anaemias, London, Oxford University Press, 1934.

anemia), the tibial marrow after the age of 7 years is unsuitable for general hematologic studies. This consideration led Seyfarth [14] to propose using the sternal marrow rather than the tibial, a suggestion which decidedly advanced the practicality of the procedure, since the sternal marrow almost never undergoes metamorphosis and remains active throughout life. Seyfarth's method of sternal trepanation has since been successfully used by such workers as Schilling,[15] Yamamoto,[16] Weiner and Kaznelson,[17] Escudero and Varela,[18] Custer,[19] Dameshek,[20] Heilbrun [21] and many others.

The trepanation method, however, has the disadvantage that it is decidedly surgical and accordingly cannot be as frequently and conveniently used as can the puncture method. Hence the introduction of the needle puncture method by Arinkin [22] may be regarded as the greatest contribution to the simplification of the technic. Arinkin proposed the use of a coarse spinal needle with a tightly fitting trochar, with which the manubrium or the body of the sternum is punctured and the marrow material withdrawn for histologic study. This method can be used as freely and easily as venipuncture is used for obtaining peripheral blood, and, according to the experience of Nordenson,[23] it can be employed on the same patient several times in the same day, if necessary, without undue discomfort to the patient. With the slight modi-

14. Seyfarth, C.: Die Sternumtrepanation, eine einfache Methode zur diagnostischen Entnahme von Knochenmark bei Lebenden, Deutsche med. Wchnschr. **49**:180 (Feb. 9) 1923.

15. Schilling V.: Das Knochenmark als Organ: II. Die feinere Zytologie des Markparenchyms, Deutsche med. Wchnschr. **51**:344 (Feb. 27) 1925.

16. Yamamoto, T.: Die feinere Histologie des Knochenmarkes als Ursache der Verschiebung des neutrophilen Blutbildes, Virchows Arch. f. path. Anat. **259**: 62, 1925.

17. Weiner, W., and Kaznelson, P.: Ueber die zellige Zusammensetzung des Knochenmarkes nach Erfahrungen mittels der Sternalpunktion nach Seyfarth, Folia haemat. **32**:233, 1926.

18. Escudero, P., and Varela, M. E.: La biopsia del midollo osseo nelle sue applicazioni in ematologia, Haematologica (II Recen.) **3**:65, 1932.

19. Custer, R. P.: Studies on the Structure and Function of Bone Marrow: III. Bone Marrow Biopsy, Am. J. M. Sc. **185**:617, 1933.

20. Dameshek, W.: Biopsy of the Sternal Bone Marrow: Its Value in the Study of Diseases of Blood Forming Organs, Am. J. M. Sc. **190**:617, 1935.

21. Heilbrun, N.: The State of the Sternal Bone Marrow in a Case of Macrocytic (Pernicious) Anemia of Pregnancy, J. A. M. A. **107**:27 (July 4) 1936.

22. Arinkin, M. J.: Methodology of Examining Bone Marrow in Live Patients with Hemopoietic Diseases, Vestnik khir. **10**:57, 1927; quoted by Young, R. H., and Osgood, E. E.: Sternal Marrow Aspirated During Life: Cytology in Health and in Disease, Arch. Int. Med. **55**:186 (Feb.) 1935; Intravitale Untersuchungsmethodik des Knochenmarks, Folia haemat. **38**:233, 1929.

23. Nordenson, N. G.: Histologiska kvantitiva studier av normal och patologisk benmärg, Hygiea **96**:193 (March 31) 1934; Studies on Bone Marrow from Sternal Puncture, Stockholm, privately printed.

fications suggested by Sonnenfeld,[24] Arjeff,[25] Baserga [26] and Reich,[27] this method has since been widely used in many clinics.

Since the development of this simplified technic of sternal puncture, the number of reports in the literature on both normal and pathologic marrow pictures has been increasing. The contributions from European clinics reported by Pokrovsky,[28] Barta,[29] Tuschinsky and Kotlarenko [30] and Tempka and Braun [31] are of special value and interest. In America the first, though brief, report was published by Holmes and Broun [32] and was followed by the slightly more extensive observations by Reich [27] and by Young and Osgood.[33] The most extensive of all the biopsy studies of bone marrow have come from Scandinavian sources (Nordenson [23] and Segerdahl [34]). Similar observations, in which the puncture technic was used, have also been reported in the Dutch literature (van der Merwe [35]). None of these workers made any attempt to standardize the marrow picture according to age periods. The observations on the marrow picture in infants reported by Kramar and Hensch [5] are not comparable with those obtained by sternal puncture, for the materials were obtained by the aspiration of marrow from the tibial diaphyses. With the simplified technic, the biopsy of sternal mar-

24. Sonnenfeld, A.: Zur Technik der Sternalpunktion, Deutsche med. Wchnschr. **54**:1380 (Aug. 17) 1928.

25. Arjeff, M. J.: Zur Methodik der diagnostischen Punktion des Brustbeines, Folia haemat. **45**:55, 1931.

26. Baserga, A.: La tecnica della sternopunctura, Riforma med. **50**:1707, 1934.

27. Reich, C.: Modified Technic for Sternal Puncture and Its Value in Hematologic Diagnosis, J. Clin. & Lab. Med. **20**:286, 1934.

28. Pokrovsky, V. I.: Das Verhältnis der Substantia reticulo-filamentosa im Knochenmark und im peripheren Blute bei verschiedenen Erkrankungen innerer Organe, Folia haemat. **39**:265, 1929.

29. Barta, I.: Die Bedeutung der Sternalpunktion bei Anämien und über die Beeinflussung des Knochenmarkes durch Leberbehandlung, Deutsche Arch. f. klin. Med. **171**:565, 1931.

30. Tuschinsky, M. D., and Kotlarenko, B. N.: Ueber Knochenmarkveränderungen bei Flecktyphus mit Bemerkungen zur Methodik der diagnostischen Punktion des Sternalmarks und der Anfertung von Knochenmarkpunktatpräparaten, Folia haemat. **46**:235, 1932.

31. Tempka, T., and Braun, B.: Das morphologische Verhalten des Sternumpunktates in verschiedenen Stadien der perniciösen Anämie und seine Wandlungen unter dem Einflusse der Therapie, Folia haemat. **48**:355, 1932.

32. Holmes, W. F., and Broun, G. O.: Clinical Study of Bone Marrow by the Method of Sternal Puncture, Proc. Soc. Exper. Biol. & Med. **30**:1306, 1933.

33. Young, R. H., and Osgood, E. E.: Sternal Marrow Aspirated During Life: Cytology in Health and in Disease, Arch. Int. Med. **55**:186 (Feb.) 1935.

34. Segerdahl, E.: Ueber Knochenmarkspunktionen, Acta med. Scandinav. supp. 59, 1934, p. 173; Ueber Sternalpunktionen, ibid. supp. 64, 1935, p. 1.

35. van der Merwe, C. F.: Beenmergonderzoek in de klinik, Amsterdam, Scheltema and Holkema, 1935; Bone-Marrow Studies in the Clinic, Folia haemat. **55**:108, 1936.

row has become a hematologic procedure easily applicable to infants and children. In the present study special emphasis was given to variations according to age during infancy and childhood.

## DEVELOPMENTAL ANATOMY OF THE HUMAN STERNUM

The human sternum develops as paired, longitudinal cartilaginous bars (mesosternal bars) from the mesenchymal mass in the ventral wall of the embryo, these bars being distinctly visible by the end of the sixth week of gestation. After the union of the cartilaginous ends of the ribs to the corresponding bars on each side, these mesosternal bands unite medially from above downward, incorporating cranially a smaller medial mass corresponding to the presternum of the lower animals (Hanson [36]). The pair of small cartilaginous masses on both sides of the presternum (coracoid procartilage) are fused with the sternal end of the clavicle, which articulates with the cranial end of the sternum (manubrium sterni). At this stage the episternal cartilage, although imperfectly separated, articulates with the clavicle, and it later fuses with the uppermost portion of the sternum, thus losing its identity (Arey [37]). During the ninth week of fetal life the two mesosternal bars are completely joined and ossification is under way (Kingsley [38]). Variations in the ossification centers are common, but usually they display a bilateral tendency, beginning with the cephalic end of the sternum and progressing downward, alternating with the ribs. Segments bearing these ossification centers are then known as sternebrae. However, the development of the sternebrae is purely secondary, having no embryologic significance. Normally, the caudal end of the sternum extends behind the last true rib, articulating with the sternum and forming the xiphisternum, or metasternum (ensiform appendix, xiphoid process). At birth the ossification centers of the manubrium are fused into one large center, while the next three segments contain small paired centers. The ossification progresses downward, the paired centers uniting into one larger center in each segment, until at the age of about 8 or 10 years ossification is so well advanced as to fill each sternebra almost completely. From this time on the sternal growth coincides with the general growth of the body, the sternum increasing in length, width and breadth (figs. 1 and 2). The fully mature sternum is anatomically divided into three parts, each separated by narrow cartilaginous bands: (1) the manubrium, (2) the gladiolus, composed of fused sternebrae, and (3) the xiphisternum. In advanced age these three parts may fuse com-

36. Hanson, F. B.: The Ontogeny and Phylogeny of the Sternum, Am. J. Anat. **26**:41, 1919.

37. Arey, L. B.: Developmental Anatomy, ed. 3, Philadelphia, W. B. Saunders Company, 1934, p. 345.

38. Kingsley, J. S.: Outlines of Comparative Anatomy of Vertebrate, ed. 3, Philadelphia, P. Blakiston's Son & Co., 1926.

pletely, leaving no discernible bands of cartilage to mark one from another.

In performing the sternal puncture on infants and children, it is essential to know the relatively correct depth to which the needle should be plunged. In order that a guide to determine this depth might be established, a postmortem study of a series of sternums from children of various ages, collected from four sources,[39] was undertaken. The anatomic measurements thus obtained may be summarized as follows:

In newly born infants the average total length of the sternum from the suprasternal notch to the tip of the xiphoid process is from 4 to 5

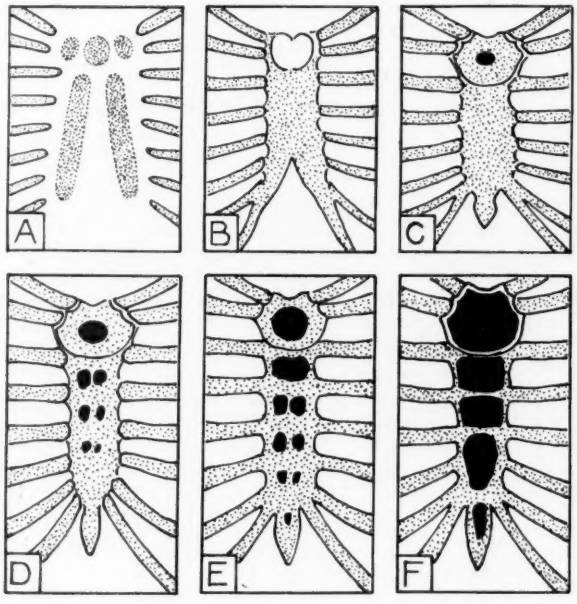


Fig. 1.—Developmental stages of the human sternum: *A*, a pair of mesenchymal bands (sternal bars) at the sixth week of gestation; *B*, union of the sternal bars during the third month; *C*, complete fusion of the sternal bands, with a beginning of manubrial ossification, at the sixth month; *D*, sternum of an infant at birth, with paired ossification centers in the upper segments; *E*, caudalward progression of ossification centers in the sternabrae, when the child is between 1 and 2 years old; *F*, complete ossification of the centers at puberty. These diagrams, redrawn and rearranged, are based on material in Kingsley,[38] Arey,[37] Piersol and Cunningham.

39. Dr. Joseph Brennemann and his associates in pathology secured material from the Children's Memorial Hospital; Dr. H. G. Wells and his colleagues in the department of pathology supplied sternums obtained at autopsies; Dr. M. Kanai obtained a similar contribution from the St. Bernard Hospital, and Dr. W. W. Cardozo and Dr. M. M. Shaw supplied material from the Provident Hospital.

cm., the width varying from 0.5 to 1 cm. and the thickness from 3 to 5 mm. When the sternum is cut through its median line, the small centers of ossification, corresponding to the marrow cavities, are usually found in the manubrium and in the first, second and third sternebrae. When one inspects the sternal plate by a transmitted light, the general outline of the centers can be clearly demonstrated; the sternum being

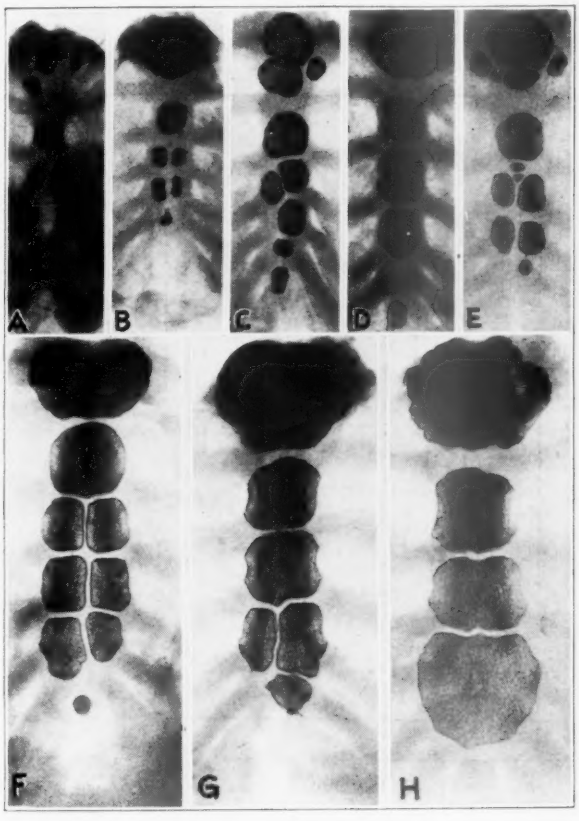


Fig. 2.—Postmortem roentgenograms of sternal plates at various ages: *A*, at 5 months; *B*, at 8 months; *C*, at 14 months; *D*, at 2 years and 9 months; *E*, at 3 years; *F*, at 4 years and 6 months; *G*, at 7 years and 4 months, and *H*, at 13 years. (These roentgenograms were supplied by Dr. William E. Anspach, the Children's Memorial Hospital, Chicago.

almost completely cartilaginous, the centers of ossification can be readily identified in it by their dark reddish areas. The utmost clearness in the visualization of these centers can be accomplished by rendering the sternal plate transparent by the method of Spalteholz.[40] The center

40. Spalteholz, K. W.: Ueber das Durchsichtigmachen von menschlichen und tierischen Präparaten, Leipzig, S. Hirzel, 1911.

in the second interspace is the marrow area utilized for sternal puncture; hence the ensuing description concerns only this center.

Of all the dimensions of this center, the most important one is its thickness in relation to the total thickness of the sternum at this location. At this level the total thickness of the sternum is composed of the anterior and posterior laminae and the marrow space between them. The numerical relations from birth to old age of the laminae to the marrow have been plotted as a scatter chart (fig. 3). The smallest sternum in the present series was that of a newly born infant who died

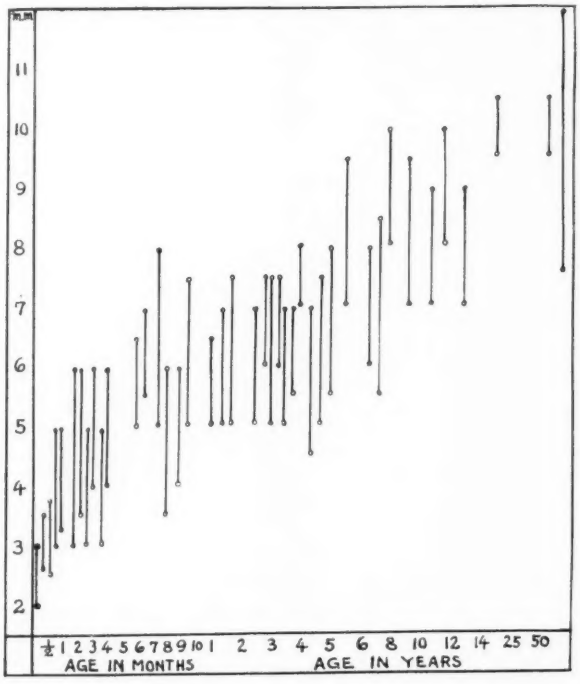


Fig. 3.—Scatter chart showing the growth of sternal thickness at the second interspace. Each measurement is represented by a vertical line connecting two readings, the top circle indicating the total thickness of the sternal plate and the bottom the thickness of the marrow tissue.

twenty minutes after birth as a result of congenital malformation of the gastro-intestinal tract. The sternal plate of this infant measured only 3 mm. in its total thickness and had an ossification center in the second interspace measuring only 2 mm. in thickness. In this study the largest sternum seen was that of an aged patient (72 years) who weighed about 200 pounds (90 Kg.) and died of carcinoma in the region of the neck on the left side; the entire length of this sternum was 24 cm.

with a total thickness at the second interspace of 1.2 cm. and a marrow cavity of 0.75 cm. Between the extremes of these two cases, the scatter chart presents a thickness gradient relative to age. According to the findings of the present study, the average maximum thickness of the sternal plate is approximately 1 cm., the thickness reached at between the ages of 6 and 10 years, which thereafter increases very little. The anterior lamina of the sternum is usually slightly thicker than the posterior lamina, the former measuring about 1.5 or 2 mm. and the latter about 1 or 1.2 mm. The entire sternum is enclosed in a firm periosteal covering; perforation of this covering with a needle is painful, making it advisable to anesthetize the tissue when performing sternal punctures.

## TECHNIC OF STERNAL PUNCTURE

In obtaining marrow material from the sternum of infants and children, preliminary knowledge of the topographic anatomy as outlined in the preceding paragraphs is requisite. The puncture may be made into the medullary cavity of either the manubrium or the second center of ossification. However, in the majority of young patients the marrow cavity in the second interspace is the most convenient of the two possible locations and is readily located between the second and the third rib, just below the usually prominent sternomanubrial ridge (angulus sterni) at the level of the second rib. The skin of the chest is first prepared in the usual manner, with tincture of iodine and alcohol. Local anesthesia is induced by infiltrating the skin, the subcutaneous tissue and the periosteum with a small amount (from 2 to 3 cc.) of a 2 per cent solution of procaine hydrochloride over the site to be punctured. A spinal puncture needle of the Barker type (fig. 4, *E*), the needle length of which has been cut down to approximately 4 cm., is gently thrust into the marrow cavity directly through the anterior lamina. In infants and young children the anterior lamina is cartilaginous, and no difficulty is experienced in entering the marrow space. Approximately 1 cm. or a little less is the average depth the needle needs to plunge below the surface of the wall of the chest to allow the aspirating needle point to reach the marrow. In older children and adults the anterior lamina, because of its increased calcification, may offer greater resistance than it does in young subjects; but a slight boring motion of the needle usually effects the entrance without much difficulty. If the resistance is too great, as in aged subjects, an easier access to the marrow cavity may be had by going through the sternomanubrial junction, as advocated by Young and Osgood.[33] The common mistake is to force the needle point in too deeply and thus to pass beyond the posterior lamina into the mediastinal space; this is particularly likely to happen

when the sternal plate is thin and entirely cartilaginous, as in very young infants. If when suction is applied no marrow is aspirated, the needle point should be slowly withdrawn, and the marrow fluid will appear in the syringe as the needle point passes through the medullary cavity. To avoid excessive penetration, some workers have attached specially devised guards to the needle (figs. *A*, *B*, *C* and *D*). It takes only a little experience, however, to judge the correct depth of penetration. Because the suction necessary for aspirating the marrow must be fairly strong, a 10 cc. Luer syringe has been found to be the most satisfactory, even though a small amount of marrow fluid (usually from 0.1 to 0.2 cc.) is all that is needed for morphologic study. Aspiration of larger

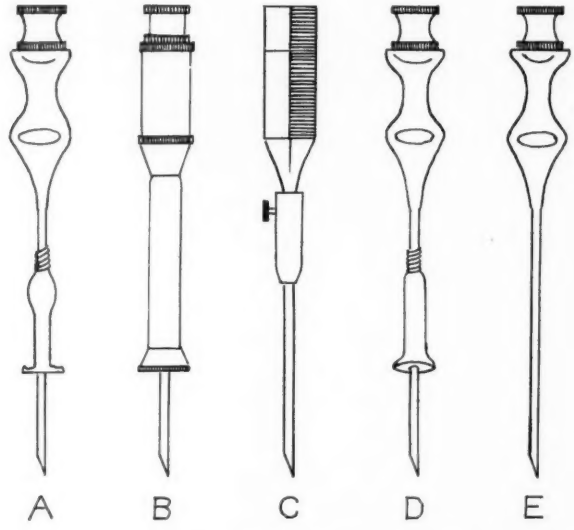


Fig. 4.—Various types of needles employed for sternal marrow puncture: *A*, Bier's needle with a guard recommended by Arinkin and modified by Arjeff; *B*, sternal needle with a mantel devised by Baserga; *C*, special needle with an adjustable guard used by Segerdahl; *D*, spinal needle with a guard proposed by Reich, and *E*, medical center Luer syringe with an improved spinal needle (Barker type), the needle length of which has been cut down to about 4 cm., used in the present study.

amounts from infants and children is inadvisable, since their marrow cavities are too small to permit the removal of material in larger quantities. Besides, aspiration of large amounts of marrow would necessarily mean admixture with it of the peripheral blood circulating in the medullary sinuses. This would be disadvantageous and confusing to the study of the essential marrow picture. Ordinarily, the aspirated fluid has the appearance of thick blood and tends to coagulate fairly quickly, which necessitates prompt smearing of the material on glass

slides in the usual manner. Some workers make use of an anticoagulant, such as heparin or an oxalate, but if smears only are to be studied no such measure is necessary. Normal marrow being rich in cells, care and skill are required to make smears thin enough for perfect staining of the cellular elements.

### FIXATION AND STAINING OF MARROW SMEARS

From 0.1 to 0.2 cc. of aspirated marrow fluid is ordinarily sufficient to prepare from ten to twelve thin smears, which, for the differential cell count, may be stained by such routine hematologic methods as the May-Grünwald-Giemsa, the Wright or the Kingsley method. Or, instead of by a usual procedure, the smears may be fixed and stained according to the method of Maximow. For the demonstration of oxidase-positive elements, the most sensitive and satisfactory staining method is that of Sato and Sekiya. If reticulocytes are to be studied, a moist preparation of a brilliant cresyl blue mixture yields the best results. When one prepares sections of the material, the marrow fluid is first allowed to coagulate in a small paper box and is then fixed for a few hours in Downey's or Helly's fluid, after which it is thoroughly washed, dehydrated, cleared and embedded in paraffin. Thin sections are then cut and may be stained by either Maximow's or Kingsley's method. It is recommended that the smears be stained not by one method alone but by several different methods in order that the observer may have readily at hand material prepared for any type of study.

### CLINICAL CLASSIFICATION OF MARROW CELLS

The classification of the various types of cells seen in stained smears of marrow fluid is both anatomically and clinically significant. The anatomic classification is necessarily minute and complex, whereas the clinical classification must be simple and practical without, of course, sacrificing accuracy of cytologic interpretation. These two groupings must be carefully differentiated, since the anatomic classification is not entirely suitable for clinical evaluation any more than the clinical classification is wholly acceptable for anatomic description. However, since the science of anatomy is the foundation of clinical hematology, the clinician must rely heavily on the achievements of the anatomists. To complicate the situation, great confusion exists as to the exact connotation of hematologic nomenclature, particularly in the interpretation of marrow cells. To repeat here the definition of the various hemocytes as previously published by me [41] is considered unnecessary, since the

41. Kato, K.: Monophyletic Scheme of Blood Cell Formation for Clinical and Laboratory Reference, J. Lab. & Clin. Med. **20**:1243, 1935

reference is easily available. For the purpose of making a differential count of the marrow smears, the following classification is believed to be adequate:

1. General (totipotential) stem cells
   (*a*) Myeloblasts (hemocytoblasts)
2. Specific (partially differentiated) stem cells
   (*a*) Leukoblasts of the granulocytic series
   (*b*) Lymphoblasts in lymphatic leukemia
   (*c*) Monoblasts in monocytic leukemia
3. Specific granulocytes (neutrophilic, eosinophilic and basophilic)
   (*a*) Promyelocytes
   (*b*) Myelocytes
   (*c*) Metamyelocytes
   (*d*) Staff cells
   (*e*) Segmented forms
4. Monocytes
   All stages are grouped together, except in monocytic leukemia, in which the different stages are separately enumerated
5. Lymphocytes and plasmocytes
   These may be listed either separately or together; in cases of lymphatic leukemia all stages may be differentiated.
6. Megakaryoblasts and megakaryocytes
7. Erythrogenic hemocytes
   (*a*) Promegaloblasts and megaloblasts in abnormal marrow, particularly in pernicious anemia
   (*b*) Proerythroblasts and erythroblasts
   (*c*) Normoblasts, both polychromatic and orthochromatic
8. Primitive cells in mitosis, the types being differentiated whenever possible

The typical cells seen in the marrow smears of a normal infant are reproduced in figure 5. Nearly all the specimens of bone marrow examined contained a certian number of rather small cells almost entirely made up of a densely staining nucleus, with little or no discernible cytoplasmic rim, some of which appeared indistinguishable from the typical small lymphocytes of the peripheral blood. Such terms as "myelogones," "erythrogones" or, more generally, "hematogones" have been applied to these elements, but in the foregoing classification they have been included, somewhat arbitrarily, with the lymphocytes. These elements may represent cells of distinct functional significance, but to enumerate them separately is at present inadvisable, since no definite knowledge exists as to their hematopoietic potency. Some authors have introduced terms such as "clasmatocytes" (Doan and Zerfas [42]), "reticu-

42. Doan, C. A., and Zerfas, L. G.: The Rhythmic Range of White Blood Cells in Human, Pathological Leucopenic and Leucocytic States, with Study of Thirty-Two Human Bone Marrows, J. Exper. Med. **46**:511, 1927.

lar, endothelial and wandering cells" (Krumbhaar and Custer [43]), "histiocytes and hemohistiocytes" (Escudero and Varela [18]), "metamyeloblasts" (Tempka and Braun [31]), "promyelocytes I and II" (Young and Osgood [33]) and even "disintegrated and smudge cells," but this nomenclature is confusing and clinically superfluous. Again, some workers apparently use the term "megaloblasts" synonymously with "proerythroblasts," but since these forms are embryologically two separate varieties of erythrogenic stem cells, such nomenclature is confusing. It will be advantageous to all workers concerned if the classification of

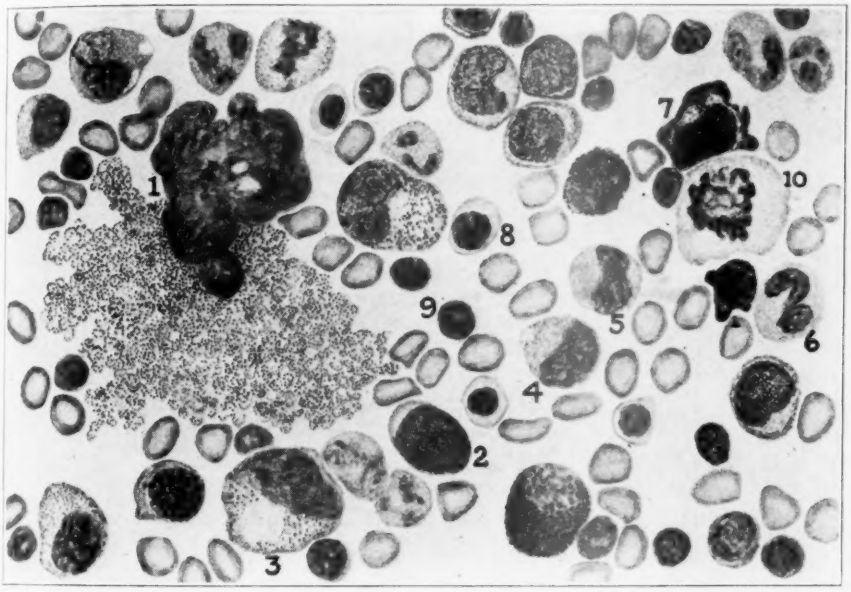


Fig. 5.—Composite camera lucida drawing of representative cells seen in the sternal marrow smear from an 8 month old infant, showing: (1) mature megakaryocyte giving off a mass of platelets, (2) myeloblast, (3) promyelocyte, (4) myelocyte, (5) metamyelocyte, (6) staff cell, (7) erythroblast, (8) normoblast, (9) small lymphocyte which may be identical with the "hematogone" and (10) primitive cell in mitosis. May-Grünwald-Giemsa method, oil immersion lens, ocular 10 ×.

marrow cells is made as simple as possible and only the cells that are definitely of clinical significance are listed.

The relationship between the erythrogenic and the leukogenic activity of the marrow has been expressed in the so-called myeloid-erythroid

43. Krumbhaar, E. B., and Custer, R. P.: A Note on the Differential Cell Count of Bone Marrow, with Special Reference to the Estimation of Infrequently Appearing Cell Types, Am. J. M. Sc. **189**:630, 1935.

ratio, calculated by dividing the total number of myelogenic hemocytes by the total number of erythrogenic hemocytes, counted simultaneously. Thus

$$\frac{M}{E} = \frac{\text{total number of myelogenic cells}}{\text{total number of erythrogenic cells}}$$

Conveniently, this rato may be calculated from the percentages as listed in the final table of differential counts (table 1). Megakaryoblasts and megakaryocytes are normally negligible in number and may therefore be listed separately. Although it is important to note and count them, the primitive cells in mitosis should not be included in either the leukogenic or the erythrogenic cell count. In leukemic marrow, in which

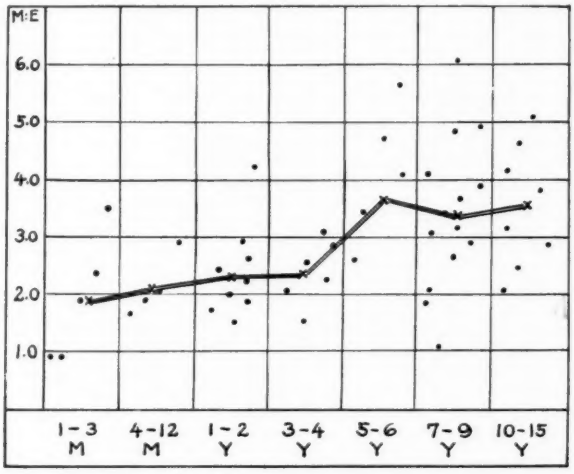


Fig. 6.—Scatter diagram showing the variations according to age in the myeloid-erythroid ratio from infancy to puberty. The curve represents the average value for each age period.

mitotic figures may be abundant, an effort may be made to study the chromosome configurations. Haploid mitosis is said to occur in leukemic blood, whereas in normal blood mitosis is diploid. Cells of the reticuloendothelial system, though important in a differential count on sections made from trephined specimens, are not usually seen in smears made from aspirated material; hence these need not be included.

## MARROW PICTURE IN NORMAL INFANTS AND CHILDREN

The interpretation of the sternal marrow picture is based on a differential count of the types of cells, exactly as in the case of peripheral blood. For this purpose it is advisable to prepare at least two good

smears from the aspirated sample of marrow fluid, the amount obtainable by the puncture technic recommended in this study being sufficient ordinarily to make ten or more thin smears. At least 500 cells are

TABLE 1.—*Summary of Average Differential Counts of Marrow Smears from Fifty-One Normal Infants and Children*

| | Age Period | | | | | | |
|---|---|---|---|---|---|---|---|
| | 1-2 Mo. | 3-12 Mo. | 1-2 Yr. | 3-4 Yr. | 5-6 Yr. | 7-10 Yr. | 11-15 Yr. |
| Number of cases | 5 | 4 | 9 | 6 | 5 | 14 | 8 |
| Myeloblasts | 2 | 2 | 2 | 1 | 2 | 2 | 3 |
| Myeloblastic leukoblasts | 4 | 2 | 3 | 3 | 5 | 2 | 4 |
| Neutrophilic promyelocytes | 5 | 6 | 9 | 8 | 10 | 4 | 4 |
| Neutrophilic myelocytes | 8 | 12 | 9 | 11 | 11 | 11 | 8 |
| Neutrophilic metamyelocytes | 9 | 17 | 11 | 10 | 13 | 11 | 10 |
| Neutrophilic staff cells | 10 | 8 | 16 | 12 | 13 | 19 | 21 |
| Neutrophilic segmented forms | 4 | 4 | 5 | 5 | 6 | 7 | 7 |
| Eosinophilic myelocytes and metamyelocytes | 4 | 2 | 4 | 2 | 3 | 4 | 5 |
| Eosinophilic staff and segmented forms | 3 | 1 | 2 | 2 | 1 | 2 | 2 |
| Basophils, all stages | 0 | 0 | 0 | 1 | 0 | 0 | 1 |
| Monocytes | 1 | 1 | 0 | 1 | 2 | 1 | 3 |
| Lymphocytes | 24 | 19 | 13 | 19 | 16 | 19 | 14 |
| Erythroblasts | 6 | 4 | 1 | 4 | 3 | 2 | 3 |
| Normoblasts | 20 | 22 | 25 | 21 | 15 | 16 | 15 |
| Myeloid-erythroid ratio | 1.9 | 2.1 | 2.3 | 2.4 | 3.7 | 3.4 | 3.6 |

TABLE 2.—*Summary of the Literature on Differential Counts of Normal Smears of Bone Marrow* *

| | Observers | | | | | |
|---|---|---|---|---|---|---|
| | Arinkin | Tempka and Braun | Holmes and Broun | Nordenson | Seger-dahl | Young and Osgood |
| Year | 1929 | 1932 | 1933 | 1934 | 1935 | 1935 |
| Number of cases | ? | 3 | 7 | 38 | 110 | 28 |
| Myeloblasts | 1.0- 2.4 | 4.6- 7.0 | 2.4 | 0.2- 5.5 | 1.3 | 0.0- 1.2 |
| Neutrophils | | | | | | |
| Promyelocytes | 1.0- 2.8 | 3.7- 6.8 | ... | 1.2- 8.2 | 1.6 | 0.0- 4.0 |
| Myelocytes | 4.5- 8.6 | 12.7-13.3 | 7.0 | 4.2- 18.0 | 14.3 | 0.0- 2.6 |
| Metamyelocytes | 1.4- 3.4 | 14.3-16.2 | 6.7 | 12.5- 42.5 | 14.8 | 1.8- 9.8 |
| Staff cells | ..... | 17.0-22.5 | 14.0 | 2.2- 10.7 | 8.3 | 15.8-33.0 |
| Segmented forms | 41.0-55.0 | 16.2-20.3 | 17.4 | 14.2- 35.0 | 25.6 | 7.4-25.2 |
| Eosinophils | | | | | | |
| Myelocytes | 0.6- 2.0 | 1.5- 3.0 | .... | 0.0- 6.2 | 1.3 | 0.0- 2.4 |
| Segmented forms | 0.6- 4.0 | 0.7- 2.5 | 1.0 | 0.2- 7.5 | 1.7 | 0.0- 1.0 |
| Basophils, all stages | 0.0- 0.7 | 0.2- 0.7 | 0.3 | 0.0- 1.2 | 0.2 | 0.0- 0.2 |
| Lymphocytes | 7.3-16.5 | 2.6- 3.3 | 24.0 | 7.5- 35.0 | 19.5 | 4.8-16.0 |
| Monocytes | 2.1- 9.8 | 0.5- 0.8 | 9.0 | 0.0- 5.0 | 2.2 | 0.0- 4.2 |
| Erythroblasts | 0.8- 2.9 | ..... | 5.2 | ..... | ... | 0.0- 4.2 |
| Normoblasts | 5.7-16.0 | 13.3-16.6 | 6.9 | 26.0-184.0 | 12.3 | 5.4 20.0 |
| Cells in mitosis | ..... | ..... | 2.9 | ..... | .... | ..... |
| Megakaryocytes | 0.6- 6.1 | 2.2- 4.0 | ... | 0.0- 1.0 | 0.04 | 0.0- 0.2 |

* The more cumbersome, disputed and confusing cell types listed in some of the reports cited are omitted. Only the well recognized cells listed in the classification proposed in the present study were included.

counted and recorded in terms of percentage of the total number of nucleated elements, including the cells of the erythrogenic series. The present study was undertaken to determine the variations in the sternal

marrow picture during infancy and childhood and to compare them with the results of similar studies reported in the literature.

A total of fifty-one normal infants and children between the ages of 1 month and 13 years served as subjects. Preliminary or simultaneous examinations of the peripheral blood, as well as careful clinical and other special examinations, were relied on to rule out the possibility that any pathologic factors influenced the marrow picture. The results of the differential counts of the bone marrow smears are tabulated in the form of a summary, in which the average values for each age group studied are given (table 1). So that the data here presented may be compared with those obtained by other investigators, a summary of the results reported in the literature is given in a separate table (table 2).

## COMMENT

The investigation of the sternal marrow of infants and children here described revealed, first, a general similarity of the picture to that reported in the literature for older age groups. However, on a careful analysis of the data, the marrow picture of young subjects was seen to differ in certain particulars from that of the older subjects. The more significant of the characteristic differences may be elaborated.

1. The most interesting and perhaps the most significant feature in the sternal marrow of young infants is the relatively low percentage of myeloid elements. In older subjects the marrow has abundant neutrophilic staff forms and, to a lesser extent, abundant metamyelocytes. In the marrow of young subjects myelocytes and, to a lesser degree, metamyelocytes form the greater percentage of the myeloid elements. Fully mature segmented forms are relatively few in number in the bone marrow of both young and old subjects, being present to the extent of less than 7 per cent. The greatest bulk of the granulocytes of the marrow consists of neutrophilic cells, but eosinophilic granulocytes, in all stages of development, are always present (from 3 to 7 per cent). Basophilic granulocytes are usually absent.

2. The relatively high percentage of lymphocytes in the marrow of young infants as compared with that in the marrow of older subjects is striking. In the marrow of infants during the first one or two months of life the small lymphocytes predominate over the myeloid elements. The majority of these lymphocytes are small, with heavily condensed nuclear chromatin and a scant amount of dark blue-stained cytoplasm. These elements, sometimes referred to as hematogones, may not be identical with the small lymphocytes of the blood, the present classification

being rather tentative, as was explained in the foregoing paragraphs. Typical blood lymphocytes of medium and large varieties are rarely found in the bone marrow of young infants.

3. The cells of the erythrogenic series display the greatest variation in number, ranging from 15 to 25 per cent of all the nucleated hemocytes. The majority of these elements can be identified as fairly mature normoblasts, the hemoglobiniferous cytoplasm varying from dark basophilic or polychromatophilic to light pinkish oxyphilic or orthochromatic hue. Among the cells of this group a number of immature proerythroblasts are always to be seen; these, together with slightly more mature erythroblasts and entirely mature normoblasts, constitute the normal erythropoietic picture of the marrow. Some of these proerythroblasts, with deep blue, somewhat granular cytoplasm, are frequently seen in mitosis. The normoblasts, on the other hand, are incapable of primary division. Karyorrhexis, Howell-Jolly bodies and the ring bodies described by Cabot are never found in the marrow of normal infants and children. Promegaloblasts and megaloblasts, also, are consistently absent from the normal bone marrow.

4. The erythrogenic elements of the bone marrow tend to approximate more closely the myelogenic elements in young subjects than in adult subjects, paralleling, perhaps, the greater erythropoietic activity of the marrow during infancy and childhood. The closer approximation between these two series of hematopoietic elements is responsible for the lower myeloid-erythroid ratio (1.9:2.4) for infants and children up to the age of 4 years, as compared with that for older children and adults (3:4). Although this ratio, even for the same age group, is subject to great variations, it may serve as a useful index of hematopoietic activity of the marrow, the ratio decreasing in value in cases of marked erythrogenic response and increasing in those of pronounced leukogenic reaction.

5. Myeloblasts, the general stem cells for all types of hemocytes (neo-unitarian school), are rather scarce in sternal marrow smears, in the present series having averaged only from 1 to 3 per cent. Only Tempka and Braun (1932) have reported a relatively high range for this stem cell (from 4.6 to 7 per cent), the majority of investigators having reported a lower average (from 1.3 to 2.5 per cent). Under normal conditions these general stem cells are probably rare, their presence being unessential since the multiplication of blood cells proceeds according to the homoplastic principle. Only in pathologic conditions does heteroplastic proliferation, which produces an abnormal increase in this type of stem cells, occur.

6. Typical monocytes of the blood are infrequently found in smears of the sternal marrow, 5 per cent for an 11 year old boy being the highest value encountered in the present series. Arinkin reported a maximum of 9.8 per cent for his series, but the average value I obtained was from 1 to 2 per cent.

7. Megakaryoblasts and megakaryocytes invariably appear in the smears of the sternal marrow, their normal number being said to be 1 to every 400 myeloid cells (Custer [19]); but in my study no attempt was made to estimate the percentage of these cells. It suffices to state that all stages in the maturation of megakaryocytes are encountered in smears of the normal sternal marrow. The fine azure granulation characteristic of the cytoplasm of mature megakaryocytes is not seen in the immature forms of megakaryoblasts, the cytoplasm of the latter being typically basophilic and distinctly granular.

8. Primitive cells in mitosis are uniformly present in sternal marrow smears. Frequently it is possible to identify the type of a certain number of these cells, chiefly from the character of their cytoplasm. Thus, in many cases erythroblasts are seen to be in this state of primary cell division, while such myeloid cells as leukoblasts, promyelocytes and even myelocytes are likewise recognizable during various phases of mitosis. Granulocytes beyond the myelocyte stage are probably incapable of primary division, since they are fully differentiated and relatively mature cells. These more mature cells may, however, undergo division by amitosis. Under normal conditions the actual number of cells in mitosis is not great, and they are therefore not included either in the differential count or in the calculation of the myeloid-erythroid ratio.

## THE STERNAL MARROW IN PATHOLOGIC CONDITIONS

It is not within the scope of this study to dwell on the details of pathologic bone marrow as examined by the method of sternal puncture. However, two cases in which the observations were fairly significant may be briefly mentioned as illustrating the specific value of this method as a diagnostic adjunct.

The first instance was that of a 2½ year old boy who came to the clinic with the complaint of enlargement of the abdomen of a few weeks' duration. On palpation, the masses were found on both sides of the flank; they were thought to be due to a renal neoplasm. Roentgenograms of the chest revealed a huge mediastinal shadow, with a sharply demarcated vertical border, extending to the midclavicular line on the right side. The peripheral blood showed no abnormalities either quantitatively or qualitatively. With a tentative diagnosis of malignancy, deep roentgen therapy was given, and the mediastinal shadow disappeared rapidly, with simultaneous reduction in the abdominal masses. The blood count at this time

was again normal as to morphology, but there was definite leukopenia (3,500 cells), which was interpreted to be the result of irradiation. About a month later, however, the child returned to the clinic with bilateral swelling of the parotid glands, which extended down both sides of the neck. Examination of the blood revealed for the first time the presence of a few myelocytes and even promyelocytes, but there was no elevation in the total count (fig. 7, A). The sternal marrow aspirated soon afterward disclosed the diagnostic picture, nearly 40 per cent of the nucleated cells being immature stem cells of the myeloid series, or myeloblasts (fig. 7, *B*). Such an observation immediately enables one to ascertain the nature of the pathologic process in the hematopoietic tissue. The second sternal puncture, performed about three weeks later, revealed that the stem cells were rapidly proliferating

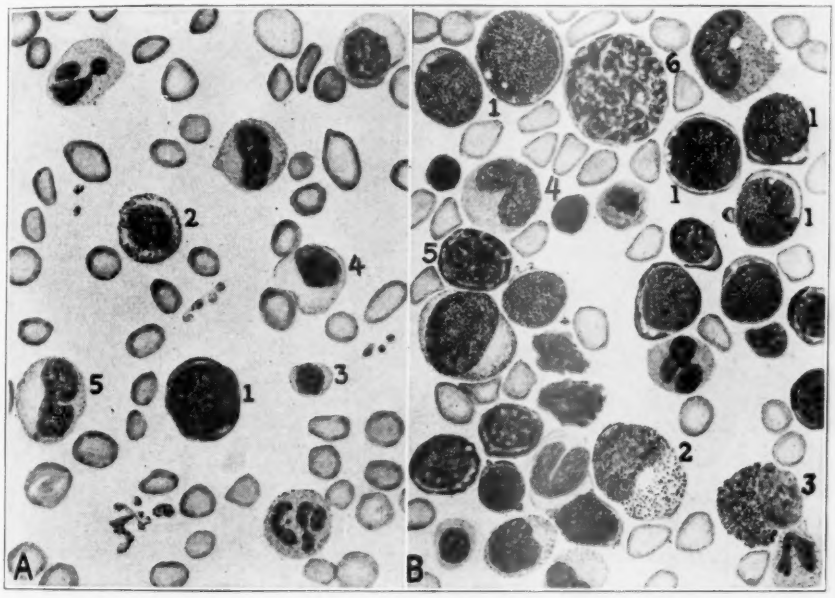


Fig. 7.—Composite camera lucida drawing of representative cells seen in smears made from (*A*) peripheral blood, and (*B*) sternal marrow material in a case of acute myeloblastic leukemia. *A:* (1) myeloblast, (2) neutrophilic myelocyte, (3) normoblast, (4) large lymphocyte and (5) monocyte. *B:* (1) myeloblast, (2) promyelocyte, (3) myelocyte, (4) metamyelocyte, (5) early normoblast, and (6) spireme formation in a myeloblast. The presence of numerous myeloblasts in the sternal marrow is diagnostic.

and now constituted approximately 90 per cent of all the marrow elements. At this time the peripheral blood showed hyperleukocytosis, the count ranging between 50,000 and 125,000, with from 60 to 75 per cent of myeloblasts, the picture typical of acute myelogenous leukemia.

The second case illustrating the value of sternal puncture as an aid to diagnosis was that of a 15 month old boy who entered the hospital with the history that the abdomen had been gradually increasing in size since early infancy. On

examination of the abdomen, both the liver and the spleen were found to be markedly enlarged. The peripheral blood showed no quantitative changes, but many lymphocytes and monocytes and a few granulocytes were observed to contain a number of large vacuoles in their cytoplasm. Some of these vacuolated leukocytes presented a honeycombed appearance due to the presence of a large number of vacuoles (fig. 8, *A*). Such a picture suggests at once the similar nature of blood cells in lipoid storage disease, as described by Pick [44] and Bloom.[45] The correct diagnosis was finally made from the biopsy of a lymph node and from the sternal marrow puncture. In the parenchyma of the lymph gland a large number of foam cells were crowding out and reducing the size of the primary lymphoid follicles; numerous foam cells were also found in the smears made from

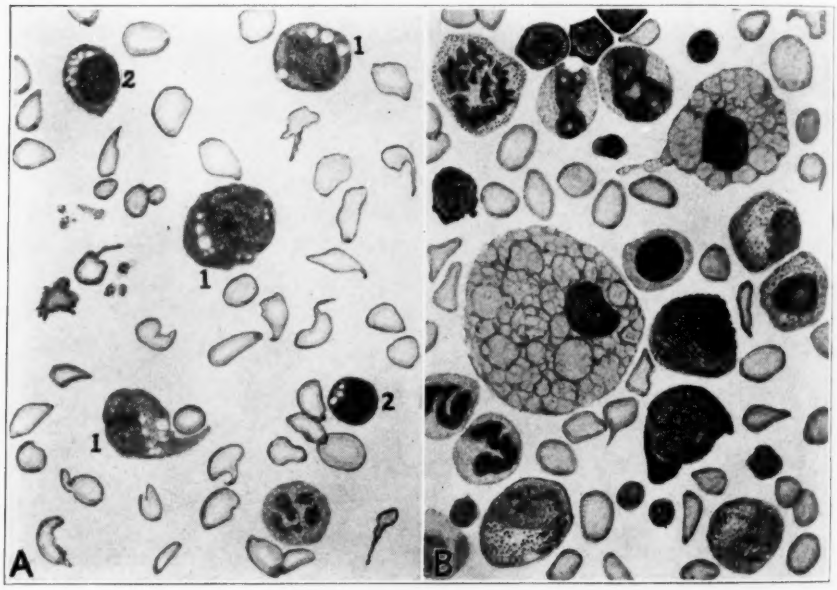


Fig. 8.—Composite camera lucida drawing of representative cells in smears made from (*A*) peripheral blood and (*B*) sternal marrow fluid in a case of Niemann-Pick's disease, showing numerous vacuoles in the cytoplasm of (*A*, 1) monocytes and (*A*, 2) lymphocytes of the peripheral blood, typical foam cells and other marrow cells in the sternal smear. Demonstration of the foam cells by the sternal puncture method was diagnostic in this case.

the aspirated sternal marrow (fig. 8, *B*). These cells were large reticular cells containing many fine spherical droplets, some of which gave a dark brick-red

44. Pick, L.: Ueber die Lipoidzellige Splenohepatomegalie Typus Niemann-Pick als Stoffwechselerkrankung, Med. Klin. **39**:1, 1927; Niemann-Pick's Disease and Other Forms of So-Called Xanthomatosis, Am. J. M. Sc. **185**:601, 1933.

45. Bloom, W.: The Histogenesis of Essential Lipoid Histiocytosis (Niemann-Pick's Disease), Arch. Path. **6**:827 (Nov.) 1928.

color reaction when treated with sudan III or scarlet red and a dark to pale blue reaction when stained with nile blue sulfate. These observations are in complete harmony with the typical pathologic changes in the tissues in lecithin or phosphatide lipoidosis of the Niemann-Pick type.

## LIMITATIONS OF STERNAL PUNCTURE

In the cytologic interpretation of marrow smears, certain obvious shortcomings inherent in the technic of sternal marrow puncture must be clearly appreciated, for example:

1. Marrow material obtained by aspiration is invariably more or less mixed with capillary and sinusoidal blood. One can minimize this admixture by withdrawing only the first 0.1 or 0.2 cc. of the material, the fluid thereafter withdrawn being increasingly mixed with peripheral blood.

2. By the aspiration method, no representative marrow picture can be guaranteed, since the more adherent cells of the reticulum and of the capillary walls are likely to be found only in abnormal numbers. Again, the lymphoid accumulations often seen around the capillaries in sectioned materials or the smaller islands of pathologic hemopoiesis may be entirely missed in aspiration.

3. The normal anatomic relations of the elements of the blood to the general structure of the bone marrow can never be studied by the puncture method.

Yet, in spite of these drawbacks, sternal puncture is well adapted to biopsy of the bone marrow in cases of certain obscure conditions, particularly in infants and in children, with whom trepanation is often difficult and inadvisable.

## SUMMARY AND CONCLUSIONS

A review of the developmental anatomy of the human sternum emphasizes the life-long hematopoietic activity of the sternal marrow, which, because of its superficial location and its relatively thin anterior lamina over the marrow cavities, is the logical tissue for biopsy studies.

Originally devised by Arinkin, sternal puncture technic has been so simplified that it may be readily employed as a routine hematologic procedure, particularly suitable in application to infants and children, on whom trepanation is more difficult to perform than on adults.

A differential cell count of nucleated elements seen in bone marrow smears made with aspirated material from infants and children reveals certain characteristics which differentiate their picture from that of the adult marrow. These differences are (1) the relatively high percentage of erythrogenic and lymphoid elements in the marrow of young subjects and (2) the relatively low percentage of myeloid elements due to a

lack of more mature granulocytes. This reversal of the percentage in erythrogenic and myelogenic elements explains the low myeloid-erythroid ratio, of 1:2, for infants and young children, older subjects normally having a value of 3:4.

The fact that the diagnosis was made possible by the sternal puncture method in a case of acute myelogenous leukemia and in a case of Niemann-Pick's lipoidosis illustrates the specific value of the method as a diagnostic procedure.

# BACTERIOLOGIC STUDIES OF AN EPIDEMIC OF PLEURODYNIA

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Macdonald and Hewell and one of us [1] have summarized elsewhere the clinical and bacteriologic observations on children in an epidemic of pleurodynia in Cincinnati. Seventy-four children suffering from this condition were admitted to the Children's Hospital during the summer of 1935. Twenty-six of this group were studied bacteriologically.

Attlee, Amsler and Beaumont [2] studied an epidemic in Eton College, England, among forty-eight boys from 14 to 18 years of age. They found "some colonies of Staphylococcus aureus and a free growth of streptococci."

Wood,[3] who saw a large number of patients, observed that blood cultures and agglutination tests for Bacillus typhosus and Bacillus paratyphosus A and B were negative and that "smears from throats showed only organisms normally present."

Churchill, Landis and Glusker [4] observed "An Epidemic of Undetermined Origin; Dengue?" in which there were fifty cases. They reported that cultures of material from the throats of eleven patients showed only the ordinary oral bacteria.

Crone and Chapman [5] observed thirty patients. They reported that the "intravenous injection, into a volunteer, of 10 cc. of whole blood from one patient on the fourth day of illness did not cause any manifest disease."

## BACTERIAL STUDIES OF CULTURES

The material for culture in our study consisted of blood from twenty-three patients, spinal fluid from three, swabs of material from the throats

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From the Children's Hospital Research Foundation and the department of pediatrics of the University of Cincinnati College of Medicine.

1. Macdonald, R. R.; Hewell, B., and Cooper, M. L.: Epidemic Myalgia, or Pleurodynia: Clinical and Bacteriologic Studies, Am. J. Dis. Child. **53**:1425 (June) 1937.

2. Attlee, W.; Amsler, A. M., and Beaumont, D. C.: Lancet **2**:492, 1924.

3. Wood, R. B.: J. Tennessee M. A. **18**:255 (Jan.) 1926.

4. Churchill, F. S.; Landis, E. M., and Glusker, S. D.: Epidemic of Undetermined Nature: Dengue? J. A. M. A. **87**:821 (Sept. 11) 1926.

5. Crone, N. L., and Chapman, E. M.: New England J. Med. **209**:1007 (Nov. 16) 1933.

of twenty-two, nasal washings from eight, Seitz filtrates of nasal washings from two and stools from eleven.

*Blood.*—A total of twenty-five blood cultures was obtained from twenty-three of the seventy-four patients. Of these, seventeen were obtained from fifteen of the twenty-six patients otherwise studied bacteriologically. An attempt was made to obtain at least 20 cc. of blood for each culture. Such blood was immediately cultured in various mediums under different oxygen tensions. Portions of each specimen of blood were cultured in anaerobic spray dishes with bactonutrient agar, $p_H$ 7.3; in tall deep tubes of brain broth (bactonutrient broth, $p_H$ 7.4, plus fresh finely ground calves' brain to a depth of 1 inch, or 33 cm.), and in deep tubes of semisolid agar (bactonutrient broth plus 0.1 per cent of agar). All cultures remained negative for at least six weeks. Three cubic centimeters of blood from one patient, a culture of which was negative, was injected intraperitoneally into a rabbit. The animal remained apparently normal.

*Spinal Fluid.*—Spinal fluid from three patients was cultured in blood-dextrose-brain broth and plain brain broth (Difco). The blood-dextrose-brain broth medium contained 5 per cent of added fresh rabbits' whole citrated blood and 1 per cent

TABLE 1.—*Incidence of Various Bacteria in Cultures of Material from the Throats of Twenty-Two Patients*

| | Number of Patients |
|---|---|
| Tiny colony, green-producing, slightly hemolytic streptococci | 22 |
| Gram-negative diplococci | 15 |
| B. influenzae | 7 |
| Staphylococci | 7 |
| Gram-positive micrococci, large | 7 |
| Slightly hemolytic gram-negative bacilli (not B. influenzae) | 3 |
| Diphtheroid bacilli | 2 |
| Hemolytic streptococci | 2 |

of dextrose. The quantities cultured were as follows: 1.5 cc. from patient V. H., 4 cc. from patient W. J. L. and 4 cc. from patient D. B. All cultures remained negative during five weeks' incubation. The spinal fluid from W. J. L. was normal as to pressure, appearance and the globulin and the cell count. The spinal fluid from patient D. B. was under slightly increased pressure but was otherwise negative. The cell count of the spinal fluid from patient V. H. showed 2 mononuclear leukocytes but was otherwise normal.

*Cultures of Material from the Throat.*—Bacteriologic studies were made of cultures of material from the throat of each of twenty-two patients. Material for culture was obtained from high in the posterior pharyngeal space by thoroughly swabbing this area with a sterile applicator. The material was cultured immediately in large tubes of the brain broth and on the surface of blood agar plates, 5 per cent of rabbits' blood being used. Table 1 shows the incidence of the different bacteria observed. The tiny colony, green-producing, slightly hemolytic streptococcus was the only micro-organism observed in the material from the throat of each patient.

These cultures of green-producing, slightly hemolytic streptococci were subjected to studies such as colony measurements and carbohydrate fermentation tests. A binocular colony microscope was used for measuring the two diameters of the colonies, the width of the green zone adjacent to the colonies and the width of the slightly hemolytic zone beyond the green zone. These measurements were obtained by making two readings at right angles to each other across the center of the

colony and across its surrounding zones of green and of slight hemolysis. In this way, as each colony was studied, four measurements were obtained on the green zone and on the slightly hemolytic zone and two diameters were obtained for the colony itself. The measurements for the zones are not diameters but widths. In table 2 such measurements are presented for the green-producing, slightly hemolytic streptococci from the cultures of material from the throats of six patients.

Data regarding carbohydrate fermentation were obtained by the use of Bacto phenol red broth base, $p_H$ 7.4, to which was added 1 per cent of the various carbohydrates. The carbohydrate reactions were observed daily for two weeks. The results are given in table 3.

TABLE 2.—*Measurements of Colony Diameters, Green Zones and Zones of Slight Hemolysis of the Green-Producing, Slightly Hemolytic Streptococci from Cultures of Material from the Throat*

| Patient | Slightly Hemolytic Zone, Width,* Mm. | Green Zone, Width,* Mm. | Colony Diameter,† Mm. |
|---|---|---|---|
| A. M. | 0.15 | 0.27 | 0.24 |
| L. | 0.15 | 0.23 | 0.32 |
| K. | 0.16 | 0.19 | 0.24 |
| R. F. | 0.15 | 0.28 | 0.27 |
| G. F. | 0.15 | 0.21 | 0.25 |
| D. C. | 0.26 | 0.22 | 0.13 |

* Average of four measurements.
† Average of two measurements.

TABLE 3.—*Carbohydrate Fermentation Tests of Tiny Colony, Green-Producing, Slightly Hemolytic Streptococci from Cultures of Material from the Throat*

| Patient | Dextrose | Saccharose | Raffinose | Mannitol | Levulose | Salicin | Maltose | Lactose | Galactose | Inulin | Bile |
|---|---|---|---|---|---|---|---|---|---|---|---|
| I. L. | A | A | — | — | A | A | A | A | A | — | — |
| N. M. | A | A | — | — | A | A | A | A | A | — | — |
| R. F. | A | A | — | — | A | ?* | A | A | A | — | — |
| D. C. | A | A | — | — | A | — | A | — | A | — | — |
| A. K. | A | A | A | — | A | A | A | A | A | A | — |
| G. F. | A | A | — | A | A | — | A | A | A | ?* | — |

* ? = variable on repetition.

*Injection Experiments on Animals.*—Table 4 shows that twenty-three rabbits were inoculated with cultures of material obtained from the throats of patients. Nine were inoculated intravenously with the original brain broth cultures, one intracerebrally with the same material and thirteen with pure cultures after isolation. All nine became acutely ill. Two died, but autopsy was not performed on either because they had been dead too long when found. The one rabbit which was inoculated intracerebrally with 1 cc. of an original brain broth culture (of material from the throat of patient J. H.) became sick quickly, had a temperature between 106 and 107 F. and died in forty-eight hours. Its lungs were deeply injected and extensively involved with early pneumonia. Sections of the lungs showed areas of acute inflammatory reaction, marked edema and congestion and some hemorrhage into the alveoli. The spleen and the liver showed marked degenerative changes. The thirteen rabbits inoculated with pure cultures of various bacteria after isolation from the cultures of material from the throat became only

TABLE 4.—*Data on Twenty-Three Rabbits Inoculated with Cultures of Material from the Throat*

| Patient | Material Injected | Amount Injected | Fate of Animal | Autopsy | |
|---|---|---|---|---|---|
| | | | | Gross | Microscopic |
| J. H. | Original broth | 4 cc. intravenously | High fever for four days; died on fifth day | No autopsy | |
| L. E. | Original broth | 5 cc. intravenously | High fever for twelve days; died on fourteenth day | No autopsy | |
| E. J. | Original broth | 5 cc. intravenously | All sick; fever; all recovered | | |
| J. H. | Original broth | 4 cc. intravenously | | | |
| M. W. | Original broth | 13 cc. intravenously | | | |
| M. T. | Original broth | 7 cc. intravenously | | | |
| E. A. | Original broth | 6 cc. intravenously | | | |
| E. A. | Original broth | 12 cc. intravenously | | | |
| J. L. | Original broth | 10 cc. intravenously | | | |
| J. H. | Original broth | 1 cc. intracerebrally | Became sick quickly; high fever; died in 48 hours | Lungs; pneumonia | Lungs, acute inflammatory reaction, edema, congestion, hemorrhages into alveoli; spleen and liver, marked degenerative changes |
| R. F. | Green streptococci | 12 cc. intravenously | Slightly sick; none died | | |
| M. W. | Staphylococci | 10 cc. intravenously | | | |
| G. F. | Green streptococci | 12 cc. intravenously | | | |
| N. M. | B. influenzae | 12 cc. intravenously | | | |
| J. H. | Gram-negative diplococci | 12 cc. intravenously | | | |
| A. K. | Green streptococci | 12 cc. intravenously | | | |
| A. S. | Gram-negative diplococci | 12 cc. intravenously | | | |
| J. H. | Green streptococci | 12 cc. intravenously | | | |
| N. M. | Green streptococci | 12 cc. intravenously | | | |
| E. G. | Gram-negative diplococci | 10 cc. intravenously | | | |
| M. W. | Green streptococci | 10 cc. intravenously | | | |
| M. W. | Haemolytic streptococci | 10 cc. intravenously | | | |
| M. W. | Gram-negative diplococci | 11 cc. intravenously | | | |

slightly sick, and none died. Of these, six were inoculated with pure cultures of the tiny colony streptococci, and seven were inoculated with various cultures representative of the other bacteria found in cultures of material from the throat.

*Nasal Washings.*—Sterile physiologic solution of sodium chloride (0.9 per cent) was used for washing the upper respiratory passages. The washings were collected in sterile basins and used immediately. Two Macacus rhesus monkeys, eight rabbits and four Swiss mice were inoculated with nasal washings. Table 5 shows the results in these animals with the exception of those in four rabbits, which remained normal.

*Monkeys Inoculated with Nasal Washing.*—Monkey 40 (table 5) was given the nasal washing from patient W. H., 2 cc. intracerebrally and 16 cc. intraperitoneally. In cultures of this nasal washing there were many of the tiny streptococci, a few gram-negative diplococci and a few staphylococci of the albus type. The monkey was fairly sick in twenty-four hours, was prostrate in twenty-eight hours and was apparently moribund in twenty-nine hours, when it was killed for necropsy. Its right lung showed early congestion. Cultures from the brain, blood and spleen gave pure cultures of tiny streptococci. On microscopic examination the spleen showed congestion and diffuse reticulo-endothelial hyperplasia in the centers of the malpighian corpuscles, the liver showed degenerative fatty infiltration and the brain showed edema and small areas of meningitis.

Monkey 49 (table 5) was given 2 cc. of the nasal washing from patient H. H. intracerebrally and 18 cc. intraperitoneally. In cultures of this nasal washing there appeared the tiny streptococci in great numbers, a few diphtheroid bacilli, gram-negative bacilli not influenza bacilli and hemolytic staphylococci (Staph. aureus). After twenty hours the monkey was breathing rapidly and was so prostrated that it did not move when touched. After thirty-one hours it appeared to be so near death that it was killed, and autopsy was performed immediately. The subcutaneous tissues of the abdomen near the point of the intraperitoneal injection were studded with many small hemorrhages. The stomach was distended. The right lung was extensively congested. No change was noticed in the diaphragm. Cultures from the blood, brain, spinal fluid, peritoneal fluid and spleen gave pure cultures of the tiny streptococci. Microscopic examination of the brain disclosed acute meningitis and edema; of the spleen, acute splenitis and reticulo-endothelial hyperplasia in the pulp and in the malpighian corpuscles; of the kidneys, moderate congestion, particularly in the capillaries of the glomeruli, and of the lungs, slight congestion.

*Rabbits Inoculated with Nasal Washings.*—Eight rabbits were inoculated with the nasal washings from eight patients. Four rabbits became sick and died. Autopsy was performed on three, and each showed gross and microscopic pathologic changes, as noted in table 5.

*Swiss Mice Inoculated with Nasal Washings.*—Four Swiss mice were inoculated with nasal washings (table 5). Two received the washing from patient W. H. One was given 1 cc. intraperitoneally and remained apparently well. The other received 0.06 cc. intracerebrally, showed no symptoms but was found dead on the fifth day. Immediate autopsy was not possible. Two other Swiss mice were given the nasal washing from patient H. H. One was inoculated intracerebrally with 0.06 cc., became fairly sick after a few hours and died in twenty-nine hours. Its right lung showed a dark red early pneumonic process, and its blood culture revealed a pure culture of the tiny streptococci. The other mouse which was inoculated intraperitoneally with 1 cc. became very sick in a few hours and died in twenty-one hours. There was free yellow purulent fluid in the abdominal cavity. Peyer's patches in the small intestine were prominent, much enlarged and deep red. Both

TABLE 5.—*Data on Animals Inoculated with Nasal Washings*

| Patient | Animal and Amount Injected | Culture of Material Injected | Fate of Animal | Autopsy | | |
|---|---|---|---|---|---|---|
| | | | | Gross | Microscopic | Cultures |
| W. H. | Monkey 40; 2 cc. intravenously; 16 cc. intraperitoneally | Green streptococci; gram-negative diplococci; staphylococci | Sick after 24 hours; moribund after 29 hours; killed after 29 hours | Lungs, early congestion | Spleen, congestion and hyperplasia of the malpighian corpuscles; liver, degenerative infiltration; brain, edema | Blood, brain and spleen, pure culture, tiny green streptococci |
| H. H. | Monkey 49; 2 cc. intracerebrally; 18 cc. intraperitoneally | Green streptococci; diphtheroid bacilli; gram-negative bacilli; staphylococci | Prostrate after 20 hours; moribund and killed after 31 hours | Right lung, congestion; petechia in abdominal wall | Brain, acute meningitis and edema; spleen, acute splenitis; kidneys, congestion; lungs, congestion | Blood, brain, spinal fluid and spleen, pure green streptococci |
| W. H. | Rabbit 1800; 1 cc. intracerebrally; 5 cc. intravenously; 15 cc. intraperitoneally | Green streptococci; gram-negative diplococci; staphylococci | Died after 23 hours; autopsy performed immediately | Right lung, diffuse congestion and hyperemia | Lung, congestion, hemorrhages into alveoli, edema of interstitial tissue and area of acute reaction | Lung, spleen, liver, duodenum and peritoneal fluid, pure green streptococci |
| H. H. | Rabbit 1792; 1 cc. intracerebrally; 5 cc. intravenously; 15 cc. intraperitoneally | Green streptococci; diphtheroid bacilli; gram-negative bacilli; staphylococci | High fever; lost weight; found dead on fifth day | ..... | No autopsy | |
| I. L. | Rabbit 1798; 1 cc. intracerebrally; 5 cc. intravenously; 8 cc. intraperitoneally | Green streptococci; gram-negative bacilli; staphylococci | Sick in a few hours; died after 21 hours | Kidneys, many small hemorrhages; lungs, hyperemia and congestion | Lung, congestion and hemorrhages into alveoli; liver, toxic degeneration; kidneys, cloudy swelling | Blood culture, negative; liver, spleen and peritoneal fluid, pure green streptococci |
| M. C. | Rabbit 1828; 5 cc. intravenously; 8 cc. intraperitoneally | Green streptococci; staphylococci; gram-negative diplococci | High fever; died on seventh day | Purulent fluid in abdomen; congestion in vessels of diphragm | Liver, congestion; spleen, congestion and hemorrhages; kidney, congestion | Abdominal fluid, pure green streptococci |
| W. H. | Swiss mouse P203; 1 cc. intraperitoneally | Green streptococci; staphylococci | Remained well | | | |
| W. H. | Swiss mouse P204; 0.06 cc. intracerebrally | Green streptococci; staphylococci | Died on fifth day | ..... | No autopsy | |
| H. H. | Swiss mouse P205; 0.06 cc. intracerebrally | Green streptococci; diphtheroid bacilli | Sick in 6 hours; died in 29 hours | Right lung, dark red | Lung, pneumonia | Blood, pure green streptococci |
| H. H. | Swiss mouse P206; 1 cc. intraperitoneally | Green streptococci; diphtheroid bacilli | Sick in 5 hours; died in 21 hours | Purulent fluid in abdomen; lungs, dark red; Peyer's patches, large and dark red | Lungs, pneumonia | Blood and abdominal fluid, pure green streptococci |

lungs were very red and resembled the picture of early infiltrative hemorrhagic pneumonia. Cultures of the blood and abdominal fluid showed only the tiny streptococci.

*Rabbits Inoculated with Pure Cultures of Streptococci from Nasal Washings.*—Six rabbits were inoculated with different cultures of tiny streptococci from nasal

TABLE 6.—*Animals Inoculated with Pure Cultures from Nasal Washings*

| Source of Material | Pure Culture | Animal and Amount Injected | Fate of Animal | Autopsy | | |
|---|---|---|---|---|---|---|
| | | | | Gross | Microscopic | Cultures |
| Blood culture, monkey 40 | Green streptococci | Rabbit B, 20 cc. intravenously | High fever; died after 42 hours | Spleen enlarged | | |
| M. L., nasal washing | Green streptococci | Rabbit 1811, 12 cc. intravenously | Sick 6 hours; killed after 33 hours | Small intestine, injected | Kidney, cloudy swelling; liver, degenerative changes | Small intestine, liver and spleen, pure green streptococci |
| M. L., nasal washing | Nongreen, nonhemolytic streptococci | Rabbit 1808, 12 cc. intravenously | Temperature, 106 F. for 6 days; died on sixth day | Negative | | |
| J. H., nasal washing | Green streptococci | Rabbit 1812, 15 cc. intravenously | Sick 5 hours; temperature, 106 F.; died after 32 hours | Lungs, dark red and congested | Lung, congestion; liver, degenerative changes; spleen, congestion, acute reaction; kidney, cloudy swelling, congestion | |
| Blood of mouse P205 | Green streptococci | Rabbit 4115DL, 1 cc. intratracheally | Fever, 5 days; moderately sick; recovered | | | |
| Blood of mouse P205 | Green streptococci | Rabbit G1813, 3 cc. intravenously | Remained well | | | |

TABLE 7.—*Measurements of Colony Diameters, Green Zones and Zones of Slight Hemolysis of the Green-Producing, Slightly Hemolytic Streptococci from Nasal Washings*

| Patient | Slightly Hemolytic Zone,* Mm. | Green Zone,* Mm. | Colony Diameter,† Mm. |
|---|---|---|---|
| W. H. | 0.27 | 0.46 | 0.22 |
| R. H. | 0.40 | 0.30 | 0.34 |
| H. H. | 0.23 | 0.15 | 0.33 |
| E. H. | 0.25 | 0.30 | 0.13 |
| H. | 0.18 | 0.15 | 0.11 |

* Average of four measurements.
† Average of two measurements.

washings. Table 6 gives the information in detail. It may be seen that five of the six rabbits became sick and four died. The gross and microscopic pathologic changes are noted in the table.

The green, tiny streptococci from nasal washings (table 7) were studied in the same way as were those from cultures of material from the throats (table 2). The measurements of the tiny streptococci from the nasal washings are given in table 7. If one compares the average of these measurements with the average of the measurements of similar streptococci from cultures of material from the throats

of these patients (table 2) one sees that there is not much difference. The colonies in the cultures of material from the throat were slightly larger, and their green and slightly hemolytic zones were somewhat smaller. The average diameter of the colonies from the nasal washings was 0.226 mm. The average width of the green zones was 0.252 mm., and that of the slightly hemolytic zones was 0.264 mm. The average for the diameter of similar colonies from cultures of material from the throat was 0.241 mm., for the green zones 0.233 mm. and for the slightly hemolytic zones 0.170 mm.

In table 8 may be seen the results of carbohydrate fermentation tests of five cultures of these streptococci.

*Seitz Filtrates of Nasal Washings.*—Two rabbits were inoculated intravenously and intraperitoneally with Seitz filtrates of nasal washings from two patients. The first received 5 cc. intravenously and 14 cc. intraperitoneally of the washing from patient J. H. The second received 5 cc. intravenously and 11 cc. intraperitoneally of the washing from patient M. C. Ten and eleven days later, respectively, the rabbits had slight febrile reactions, but otherwise they remained normal. All cultures of Seitz filtrates remained negative for six weeks.

TABLE 8.—*Carbohydrate Fermentation Tests of Tiny Colony, Green-Producing, Slightly Hemolytic Streptococci from Nasal Washings*

| Patient | Dextrose | Saccharose | Raffinose | Mannitol | Levulose | Salicin | Maltose | Lactose | Galactose | Inulin | Bile |
|---|---|---|---|---|---|---|---|---|---|---|---|
| W. H. | A | A | — | — | A | A | A | A | A | — | — |
| R. H. | A | A | — | — | A | — | A | A | A | — | — |
| H. H. | A | A | ?* | A | A | A | A | A | A | ?* | — |
| E. H. | A | A | — | — | A | A | A | A | A | — | — |
| J. H. | A | A | — | — | A | A | A | A | A | — | — |

* ? = variable on repetition.

*Studies of Stools.*—Stools from eleven patients were studied bacteriologically. All contained Bacillus coli, six contained Streptococcus faecalis and five contained Bacillus lactis-aerogenes.

Saline suspensions of two stools were injected intraperitoneally into two rabbits, each receiving 2 cc. One rabbit died, showing enlarged mesenteric glands, cultures of which revealed B. coli. Culture of the injected material revealed B. coli, Str. faecalis and B. lactis-aerogenes.

## COMMENT

These studies show that tiny colony, green-producing, slightly hemolytic streptococci were the only micro-organisms observed in the pharyngeal cultures of the patients we studied. We do not conclude, however, that this evidence has any significance in regard to the etiology of pleurodynia. Our experience with cultures of material from the throat in this community during the past several years shows that practically all such cultures contain green-producing, slightly hemolytic streptococci. We feel that this group of streptococci is at present practically impossible of differentiation by cultural and morphologic studies. Studies with animals occasionally assist in showing that some organisms have the ability to localize in certain tissues. In attempting to obtain

additional information regarding cultural characteristics, we utilized in this study a method of measuring not only the size of the colonies but the bands of green and of slight hemolysis surrounding the colonies.

SUMMARY

Twenty-six patients suffering from a condition clinically diagnosed as pleurodynia were studied bacteriologically. The material studied was blood, spinal fluid, cultures of material from the throat, nasal washings, Seitz filtrates of nasal washings and stools.

Two monkeys, forty-one rabbits and four Swiss mice were inoculated with the original material from the patient, with original cultures or with pure cultures after isolation. The injections resulted in the death of two monkeys, twelve rabbits and three Swiss mice.

The only micro-organism observed consistently in material from the upper respiratory tract of all the twenty-six patients was a slightly hemolytic green-producing streptococcus.

In defining the cultural characteristics of this group of green-producing streptococci more clearly, we measured not only the size of the colony but the width of the bands of green and of slight hemolysis produced by the colony.

Twenty-five blood cultures from twenty-three patients failed to show any bacterial growth during six weeks' incubation.

Three spinal fluid cultures also failed to show any growth during six weeks' incubation.

In two rabbits inoculated with Seitz filtrates of nasal washings, fever developed on the tenth and the eleventh day, respectively.

All cultures of Seitz filtrates of nasal washings remained negative for six weeks.

Cultures of stools showed no unusual bacteria.

The most frequent pathologic observation on the animals studied at necropsy was deep red, diffuse and spotty congestion seen grossly in the lungs, which when studied microscopically showed congestion, hemorrhage, edema and acute cellular reactions. Sections also showed toxic changes in the livers, spleens and kidneys.

Although these studies furnish additional information concerning the characteristics of green-producing streptococci, no evidence is presented that they have any relation to the etiology of pleurodynia.

# THE MORO REFLEX

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One of the prominent behavior patterns characteristic of the newborn infant is the Moro reflex, or body-startle response. This activity was first described by Moro,[1] in 1918.

Early literature on the subject was concerned primarily with enumerating different stimuli which would elicit the reaction or with the clinical implications of the reaction pattern. Moro's method of stimulation consisted in striking forcefully the table or bed on which the infant was lying in a supine position. Ordinarily the blow was made simultaneously on both sides of the baby, about 6 or 8 inches (15 or 20 cm.) from his head. This method has remained the classic mode of stimulation. However, Schaltenbrand [2] and Freudenberg [3] pointed out that many other types of stimuli provoke the same pattern of action. Some of the stimuli used are tapping on the abdomen, blowing a gust of air on the face, rapid transfer of the bodily position, dropping the body through space several inches and cold or warm applications to the chest or abdomen. This list of possible stimuli suggests that it is the quality of suddenness in the stimulation which is most likely to evoke the typical Moro reflex.

According to Moro the reflex is comprised of movements primarily in the upper extremities—a bilateral spreading of the arms outward from the body followed by their approaching each other in the form of a bow. Extension and adduction of the lower extremities frequently accompany the extensor movement of the arms. Moro likened the reflex to the "clasping instinct" of primates, which was first described by Dorflein. He expressed the belief that the reflex as observed in infants is the

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1. Moro, E.: Das erste Trimenon, München. med. Wchnschr. **65**:1147-1150, 1918.

2. Schaltenbrand, G.: Normale Bewegungs- und Lagereaktionen bei Kindern, Deutsche Ztschr. f. Nervenh. **87**:23-59, 1925.

3. Freudenberg, E.: Der Morosche Umklammerungsreflex und das Brudzinskische Nackenzeichen als Reflexe des Säuglingsalters, München. med. Wchnschr. **68**:1646-1647, 1921.

residue of a strong and useful reflex in the prehuman ancestors of man. No other outstanding theories as to its origin and purpose have been proposed.

Recent studies have dealt largely with the frequency of occurrence of the reflex in a given infant population.[4] Diagnostic use of the reflex as a clinical device was suggested by Gordon [5] and Sanford.[4a] Gordon expressed the opinion that an asymmetrical pattern indicated motor paralysis or injury on one side and that persistence of the reflex signified cerebral or pyramidal injury. Sanford,[4a] on the other hand, stated that in new-born infants over 24 hours of age an asymmetrical response was strongly suggestive of a fractured clavicle.

Authors seem to agree that the reflex is strongest in the new-born, and that it tends to weaken or disappear by the time the child is several months old. Many writers, among them Gordon,[5] Dupérie and Bargues [6] and Moro [7] expressed the belief that persistence of the pattern beyond a certain age signifies a neuropathologic lesion or mental retardation. Dennis,[8] on the other hand, contended that the so-called disappearance of the reflex is an artefact in the condition of the experiment. He claimed that the older infant, being conditioned to the situation, anticipates the blow, tenses his muscles and thereby inhibits the reflex response. Peiper,[9] too, alleged that the pattern is often shown in normal older children if they suddenly start to fall.

Sequential phases in the form of the behavior pattern as it tends toward evanescence were first analyzed by me.[10] The nearest pre-

4. (*a*) Sanford, H. N.: The Moro Reflex as a Diagnostic Aid in Fracture of the Clavicle in the New-Born Infant, Am. J. Dis. Child. **41**:1304-1306 (June) 1931. (*b*) Rolando, F.: I riflessi del neonato normale, Pediatria **39**:645-650, 1931. (*c*) Irwin, O. C.: The Latent Time of the Body Startle in Infants, Child Development **3**:104-107, 1932. (*d*) Chaney, L. B., and McGraw, M. B.: Reflexes and Other Motor Activities in Newborn Infants: A Report of One Hundred and Twenty-Five Cases as a Preliminary Study of Infant Behavior, Bull. Neurol. Inst. New York **2**:1-56, 1932.

5. Gordon, M. B.: Moro Embrace Reflex in Infancy: Its Incidence and Significance, Am. J. Dis. Child. **38**:26-34 (July) 1929.

6. Dupérie, R., and Bargues, R.: A propos des réflexes inconditionnels du nourrisson: Le réflexe de l'étreinte de Moro, Gaz. hebd. de sc. méd. de Bordeaux **53**:66 (Jan.) 1932.

7. Moro, E.: Zur Persistenz des Umklammerungsreflexes bei Kindern mit zerebralen Entwicklungshemmungen, München. med. Wchnschr. **67**:360, 1920.

8. Dennis, W.: A Psychologic Interpretation of the Persistence of the So-Called Moro Reflex, Am. J. Dis. Child. **50**:888-893 (Oct.) 1935.

9. Peiper, A.: Die Hirntätigkeit des Säuglings, Berlin, Julius Springer, 1928, p. 101.

10. McGraw, M. B.: Growth: A Study of Johnny and Jimmy, New York, D. Appleton-Century Company, Inc., 1935.

vious approach to an analysis of the sequential change appeared in Freudenberg's [3] article, in which he pointed out that stretching and spreading of the upper extremities are retained after the adductor movements have faded. Gordon,[5] who studied some of the infants in his investigation during the first five or six months, when the reflex is most active, did not analyze the progressive changes in the form of the pattern.

The following account of developmental sequences is based on a study of 57 infants from birth to the age of 8 or 10 months. This study offers more tangible data than my previous descriptive analysis. A total of 751 observations were recorded on the 57 infants. Of these observations, 270 were movie records and 481 were written descriptions made at the time of stimulation. It was not possible to hold the interval between observations constant, but in general it was approximately two weeks. The greatest number of observations made on any child was 37, the number made on most of the children being 10.

The method which we used for the purpose of stimulating the reaction pattern varied slightly from the classic manner described by Moro. Instead of striking simultaneously on both the right and left side of the child's head, we struck a forceful blow with a long stick on the mattress on which the infant was lying, about 6 inches (15 cm.) from the top of his head. The infant was lying in the customary supine position. The bodily movements of the baby, obviously in response to the stimulation, were recorded by descriptive notes or by cinema. In making descriptive notes we analyzed the movements according to various bodily segments, that is, as movements of the head, trunk, lower extremities or upper extremities. We never recorded the reflex as merely present or absent. This manner of recording minimized the influence of any preconceived notion as to the nature of the reaction pattern.

Although there are wide individual differences both as to the intensity of the reaction and as to the details of the form of the behavior pattern, the essential character of the reflex is sufficiently constant to render an analysis of the developmental changes both possible and warranted. The most prominent feature of the reaction of the new-born infant is a bilateral extension and abduction of the upper extremities which ends in a bowing of the arms over the thorax before the original position of flexion and abduction is resumed. Simultaneously there is an extension of the spine, often involving a retraction of the head toward the interscapular part of the spine and a rolling of the body slightly to one side. The digits tend to extend and to fan, with the exception of the distal phalanges of the index finger and the thumb, which are flexed, thus forming the shape of a "C." The position of the lower extremities immediately before stimulation determines in large measure their responsive movements. If the lower extremities are flexed and abducted, which is their most characteristic posture with the new-born

infant, the direct response is most often a slight flexor movement followed by a large bilateral extensor thrust. If, however, the legs are slightly extended before stimulation, the initial flexor movement is more gross. The composite of these several bodily movements (i. e., extension and bowing of the arms, extension of the spine, extension and fanning of the digits and extension of the legs) we have called the initial, or new-born, phase. During this phase the motor response is usually followed by intense crying.

Development during the second or third month is indicated by a gradual diminution of the grosser movements in response to sudden

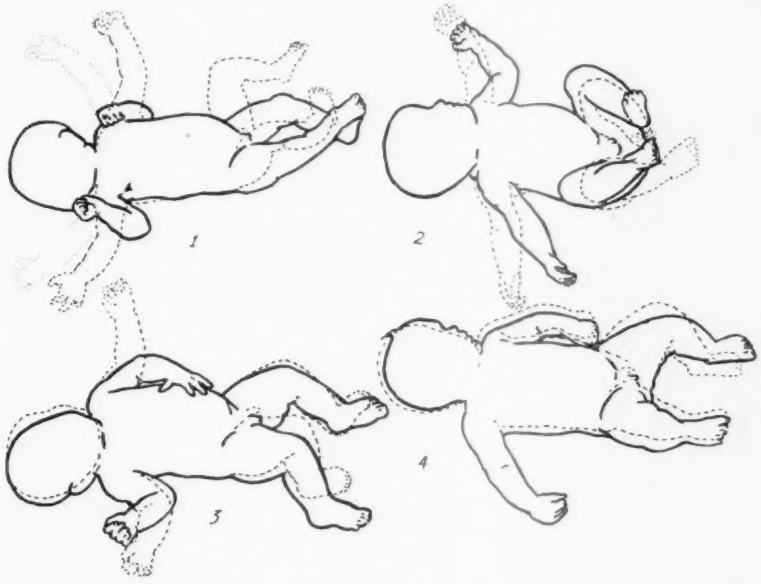


Fig. 1.—Line drawings which illustrate the somatic movements in the several phases of the Moro reflex (from McGraw, M. B.: Growth: A Study of Johnny and Jimmy, New York, D. Appleton-Century Company, Inc., 1935).

stimuli. The bowing of the upper extremities and the spinal extension become noticeably reduced, until finally the baby remains flat on his back and merely extends and abducts the upper extremities. The expanse of movement in the lower extremities is greatly diminished, the movement often being little more than a gross jerk which brings the knees together or apart. The associated crying is less frequent and less intense. Sometimes the child tenses the facial muscles as if to cry but does not actually do so; blinking of the eyelid has usually appeared by this time. A gross jerk of the head or the upper part of the trunk may be present, or the body may remain inactive. This type of reaction we have called the second, or transitional, phase of the behavior pattern.

*Suggested Form for Use in Checking the Essential Features of the Response During Any Phase*

| | |
|---|---|
| I. Position and Attitude Before Stimulus | |
| Upper extremities flexed and abducted | |
| Lower extremities flexed at knees and abducted | |
| Spine on surface | |
| Quiet | |
| Upper extremities extended, resting by side, or flexed on trunk | |
| Lower extremities extended | |
| II. Stimulus-Response | |
| (*a*) Upper Extremities | |
| Bowing: Upper extremities brought above body | |
| Unilateral Bilateral | |
| Upper extremities extend, move outward from body | |
| Gross unidentifiable movement in upper extremities | |
| Upper extremities drawn toward body in quick movement | |
| No overt movement in upper extremities | |
| Digital extension | |
| "C" posture * | |
| No overt movement in digits | |
| (*b*) Body | |
| Spine extended—body turns laterally | |
| Spine remains entirely on the surface | |
| No movement in trunk | |
| Quick jerk of head (not in trunk) | |
| Gross body jerk | |
| Fine body jerk | |
| Blinking | |
| (*c*) Lower Extremities | |
| Lower extremities extended Unilateral Bilateral | |
| Lower extremities flexed Unilateral Bilateral | |
| Flexion of lower extremities, immediately followed by extension | |
| Extension of lower extremities immediately followed by flexion | |
| No overt movement (apparently not sensitive to stimulus) | |
| (*d*) Affective | |
| Intense crying | |
| Motor response precedes vocal response | |
| Vocal response precedes motor response | |
| Tension of facial muscles as if to cry—no actual crying | |
| No suggestion of crying | |
| No somatic response detectable (sensitive to stimulus but somatic movement suppressed) | |

* "C" posture is described in the text.

As the child continues to grow, the amount of overt somatic activity becomes even less. At last practically all gross movement seems to be suppressed, and the characteristic reaction consists of a fine body jerk associated with blinking. Usually the child does not cry. We have termed the body jerk the final, or mature, phase, since it is the characteristic startle response even of adults. Sometimes the jerk is so fine that although felt by the subject it cannot be detected by an observer.

The line drawings in figure 1, which were made by tracing 16 mm. movie film frames, illustrate the somatic movements in the several phases, as described. The table offers a convenient scheme for checking the essential features of the response during any phase. Such a checking system, although reducing the confusion which arises from descriptive notes, is useful only in the hands of a skilled observer. Furthermore, such a method of checking cannot take into account the range of individual differences. We were not concerned so much with individual variations as with the consistent changes in the form of the activity as a function of development. It may be said that the essential aspects of the reaction pattern, which are sufficient to identify the phase of development of this activity at which a child may be functioning at a given time, can be recorded in this way, provided the more expensive cinema technic cannot be employed.

The classification of the behavior pattern into the three phases mentioned is based on the empirical judgment of the investigator. The same observer passed judgment in every instance. Naturally some babies achieve the mature type of reaction much earlier than others. It may be seen in figure 2 that the outstanding changes occurred in the greatest number of the 57 infants whose development we studied when they were about 90 days old and when they were about 130 days old. The largest percentage of infants shifted from the first to the second phase when they were about 90 days old; the largest percentage changed from the transitional to the mature phase when they were about 130 days old. All the infants had passed from the first to the second phase by the one hundred and thirtieth day, and they had all passed from the transitional to the mature phase by the two hundred and tenth day. These figures suggest that if a well child manifests the typical bowing pattern of the new-born beyond the age of 4½ or 5 months and shows gross diffuse somatic movements along with the body jerk after the age of 7 months, inquiry concerning possible factors influencing his development in this respect is advisable. We have not studied in any way the clinical application of this behavior pattern as a possible indication of retardation. Whether the reflex is observed for clinical or for research purposes, to indicate merely its presence or absence is inadequate.

The age limits within which a phase occurs are determined by judgment of several factors which enter into each response. The actual developmental trend of the behavior pattern is perhaps better revealed when each factor is considered separately, as shown in figure 3. These curves represent an analysis of the same data as those of figure 2, but each item or component is handled on a plus or minus basis and is then plotted in terms of percentages. For example, what percentage of the subjects between 1 and 10 days of age showed the pattern of bowing of the upper extremities over the thorax? The curve for this aspect of the reaction pattern begins rising at the tenth day and continues rising

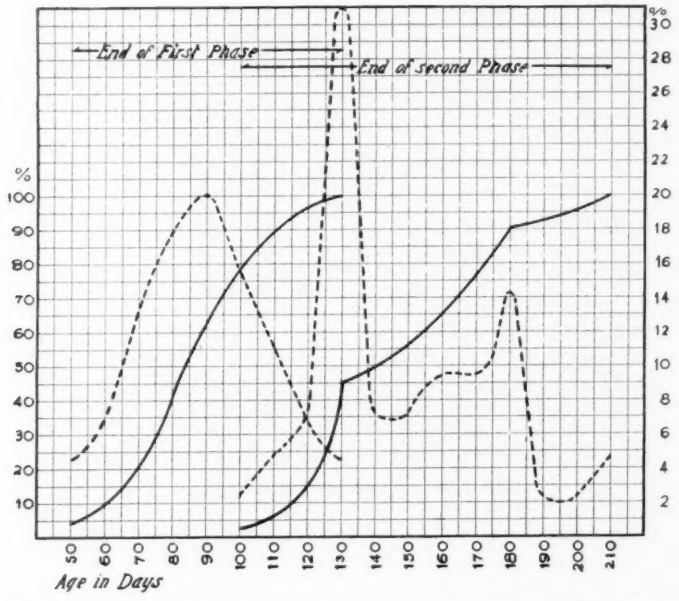


Fig. 2.—Curves illustrating the period of maximum phase change of the Moro reflex. The solid lines indicate the total percentage of the first and second phases completed, and the broken lines, the percentage of the first and second phases completed at different ages.

until the thirtieth day, when the decline sets in, and the decline continues fairly steadily until the one hundred and twentieth day. The curve for extension of the lower extremities and spinal extension follows the same general trend. Crying is distinctly a part of the pattern during the early months, and the shape of the curve for crying follows the same course as that for the other three aspects, but after the age of 150 days, when the body jerk has become the more established type of reaction, crying represents the infant's general adjustment to the laboratory situation rather than a definite component of the reaction

pattern. The curve for the reaction designated as body jerk begins to rise at about 40 days and reaches its peak at 165 days. The decline which follows represents not an actual decline in this aspect of the behavior pattern but an adaptation of the child to the particular stimulus which was used in the experimental "set-up." The curve for extension of the upper extremities represents the transition from the bowing, or classic reflex behavior, to the more mature body jerk response. The curves drawn from these data are representative of the trends shown

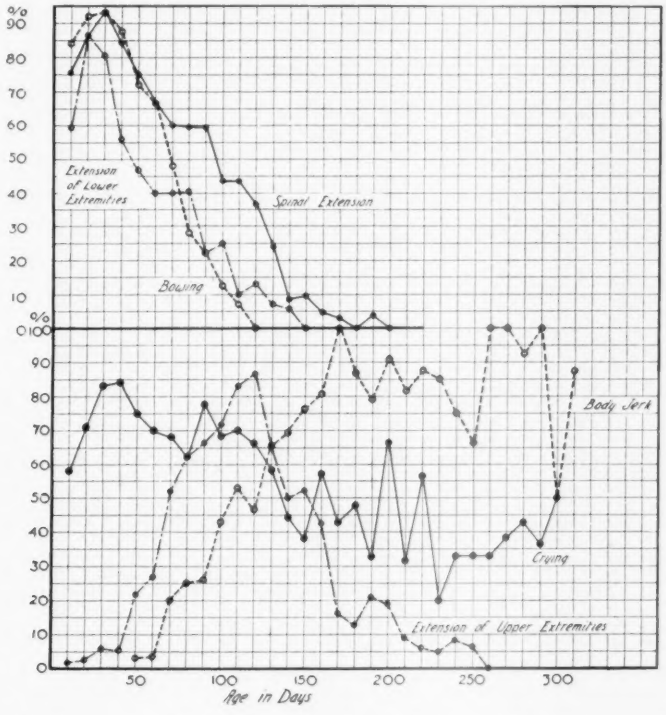


Fig. 3.—Occurrence of the component parts of the Moro reflex, in percentage.

by the major components of the behavior pattern charted as a function of chronological age. The primary disadvantage of curves derived in this manner is that the original data must be recorded on a positive or negative basis. Development is never "all" or "none." It is always a matter of "more" or "less." Both curves dealing with changes in the form or character of the behavior fail to delineate differences of degree.

Within a certain measure, differences in the intensity or degree of reaction were calculated by counting the number of 16 mm. movie frames involved in photographing the reaction. The black line in the curve in figure 4 represents the average duration of the response for

respective ages; the shading indicates the variability. These data represent the duration of the total response and not the various components involved in the behavior pattern. One glance at the curve reveals a definite rise in the duration of the response during the first month. On the whole, this rise amounted to approximately three and two-tenths seconds. During the second month there was a sharp decline of about two seconds. It has been remarked that a noticeable change occurs around the ninetieth day. I have elsewhere stated [10] that a declining aspect of development frequently shows a flare-up before a marked change occurs in the process of development. This flare-up is shown quantitatively in the curve by the rise of four-tenths second in the dura-

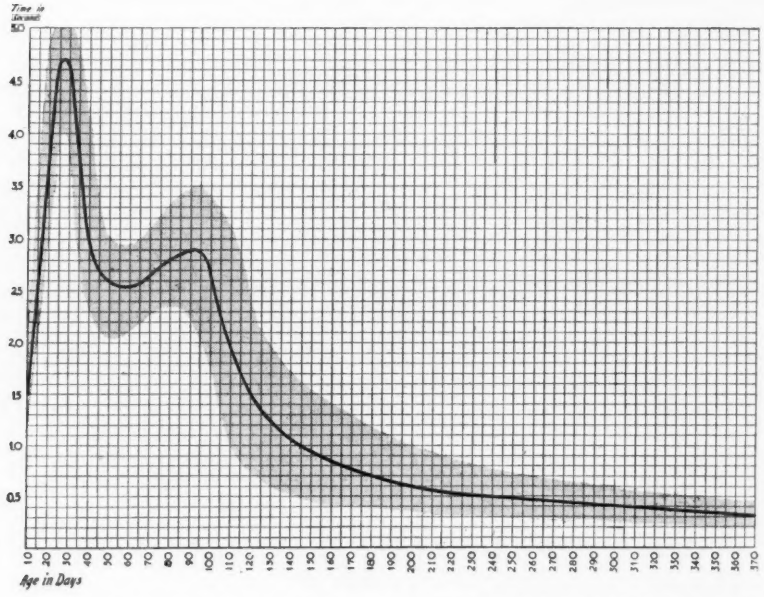


Fig. 4.—Duration of the Moro reflex (group curve). The black line indicates the average duration for the different ages, and the shading, the variability.

tion of the reaction between the ages of 60 and 90 days. The composite curve shows a rapid steady decline from the ninetieth day onward. There is a decrease of one and seven-tenths seconds between the ages of 90 and 130 days and of five-tenths second between 130 and 180 days, but of only fifteen-hundredths second between 180 and 210 days. In other words, by the age of 180 days the pattern has become fairly well stabilized. Individual curves, as shown in figure 5, tend to show a second flare-up before the final decline. If we had had sufficient data calculated from movie film this second flare-up would probably show in the composite curve also. Increased variability when the child is between 130

and 150 days old is indicated on the composite curve by shading. Systematic daily records of the same infants are necessary to elucidate the characteristic rhythms and variations.

As one observes progressive changes in a relatively simple behavior pattern, so simple and constant as to be called a reflex, one cannot help wondering what has happened in the child's functional organization to effect such outstanding behavioral changes within the first few months of life. Moro [7] and Freudenberg [3] claimed that a persistence of the reflex beyond the sixth month indicates maldevelopment of the pallidal

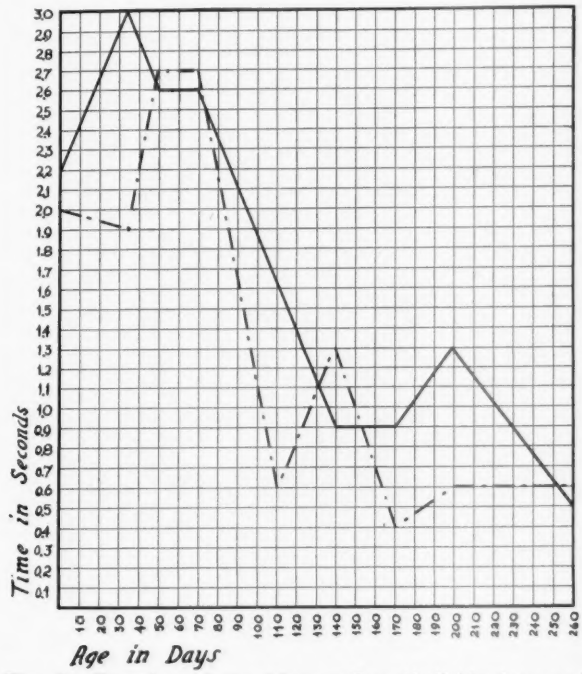


Fig. 5.—Duration of the Moro reflex (individual curves).

area and the pyramidal tracts. Beyond this assertion no one has as yet attempted to relate the reflex to definite structural mechanisms or to construct an adequate theoretical explanation for its apparent diminution during development. Most of the earlier writers merely stated that normally the reflex disappears. They made no effort to explain what became of it when it disappeared or what reorganization in the nervous system of the child made such changes in behavior possible. Dennis [8] implied a neural reorganization when he contended that the tenseness of the older child inhibits the reflex responses, the tenseness being attributed to the baby's advanced powers in understanding and anticipating the stimulus.

Studies on the nervous system which Dr. Frederick Tilney has under way seem to indicate that the cortex is not functioning to any appreciable degree at the time of birth. The subcortical nuclei would therefore be in charge of all somatic musculature in the new-born. Predominating somatic activity at this period is of the flexor type. Although the neural centers governing the reflex are of the nuclear level, the significant somatic movement in the early phase of the Moro reflex is of the extensor type. The reaction appears to be a residual defensive or protective response. The gross extensor movements, characteristic of the new-born phase, serve to facilitate greater power in the flexor expression. So far as the nervous system is concerned, the total muscular reaction means the activation of all motor groups in the neuraxis caudal to the midbrain. That is to say, it represents a flooding of the motor segments with nerve energy which expends its force on motor agents through the intersegmental association fibers in all the segmental levels of the neuraxis. Definite pathways are not established; so any sudden stimulus may set off a diffusion of nerve impulse throughout the entire neuraxis up to the midbrain.

During the second phase myelinization appears to be taking place in the cord and the brain stem. This myelinization would mean that neural pathways are becoming more definitely linked together. Such an organization of pathway systems could account for the reduction in diffuse somatic response.

By the time the child has achieved the body jerk, or mature phase, the cortex is definitely engaged, practically at the instant of the startling stimulation. Before the subject has had time to perform a complete reflex, cortical inquiry as to the meaning of the startle is activated. However, the nuclear level continues to function when the subject is taken by surprise even in maturity, but cortical inquiry, which sets in immediately, serves to restrict the nuclear aspect of the reaction to a body jerk. Further somatic activity follows cortical deliberation, or inquiry concerning the nature of the stimulus.

Since the response to startle, even in the mature phase, remains a combination of cortical and nuclear activity, the Moro reflex is an early behavior pattern which lends itself conveniently to the study of cortical development. The reflex is a distinct behavior pattern which undergoes sequential developmental changes during the early months of postnatal life. It may therefore conveniently be used not only for elucidating the developmental course of the reflex itself but for the determination and improvement of methods for recording and handling data concerning other types of behavior development.

SUMMARY

In a study of the Moro reflex in infants it is inadequate merely to record the reflex as present or absent. The reflex passes through significant developmental changes, which are described in detail. Means of recording and handling data so as best to show the character of these changes are described. The basic structures of the nervous system which govern the reaction at the various developmental stages are briefly discussed, and the value of the reflex as a tool for the study of the cortical development is indicated. Since the Moro reflex is a type of behavior which undergoes fairly well established changes during the early months of postnatal life, it affords a useful means of studying other physiologic processes of growth.

# UTILIZATION OF ORGANIC AND INORGANIC IRON BY THE NORMAL INFANT

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In this study the relative availability of inorganic and of organic iron in the diet of the normal infant has been investigated by means of a study of the iron balances over a long period. Interest in the problem was stimulated by the reports of Elvehjem and his colleagues,[1] which indicated that in the case of rats only the inorganic portion of the dietary iron was utilized.

Until now practically all investigators interested in determining the "availability" of organic and inorganic or ionizable iron for hemoglobin synthesis have used anemic rats for their feeding experiments. Elvehjem and his co-workers [1] found consistently that in the case of the anemic rat only the inorganic portion of the iron in the diet is utilized for the formation of hemoglobin. They found this to be true when a number of foods were given and the hemoglobin response was compared with that manifested when amounts of ferric chloride equivalent in some experiments to the total iron, and in others to the inorganic iron, of the food were given. Since organic iron occurs in animal and in plant foods in the form of hematin or hematin-like compounds, Elvehjem [2] also fed iron in the form of hematin. The hemoglobin showed no gain, and analyses of the livers of the experimental animals showed that no iron had been stored in them. This indicated the inability of the

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From the Departments of Pediatrics and Home Economics of the University of Chicago. The study was supported in part by a grant from the Douglas Smith Foundation for Medical Research of the university.

1. (*a*) Elvehjem, C. A.; Hart, E. B., and Sherman, W. C.: The Availability of Iron from Different Sources for Hemoglobin Formation, J. Biol. Chem. **103**:61 (Nov.) 1933. (*b*) Sherman, W. C.; Elvehjem, C. A., and Hart, E. B.: Further Studies on the Availability of Iron in Biological Materials, ibid. **107**:383 (Nov.) 1934. (*c*) Elvehjem, C. A.; Hart, E. B., and Sherman, W. C.: The Limitations of Cereal Milk Diets for Hemoglobin Formation, J. Pediat. **4**:65 (Jan.) 1934.

2. Elvehjem, C. A.: The Relative Value of Inorganic and Organic Iron in Hemoglobin Formation, J. A. M. A. **98**:1047 (March 26) 1932.

rat to assimilate the iron of the hematin molecule. From findings in the various studies to which reference has been made, Elvehjem and his associates concluded that only the inorganic portion of the iron of food was utilized.

Vahlteich, Rose and MacLeod,[3] however, did not agree with that conclusion. When they fed whole wheat (which is reported by Elvehjem to have only 47 per cent of its iron in the inorganic form) to anemic rats, they found a hemoglobin response comparable to that when they fed ferric chloride equivalent in amount to the total iron in the whole wheat, the copper content of the diets being constant. When the wheat was predigested before it was used, they found a higher hemoglobin response than with ferric chloride. They considered digestibility to be a factor in very young and very anemic animals.

Widdowson and McCance [4] calculated the total intake of iron and the intake of inorganic iron of a number of adults whose diets were weighed. In one group the inorganic iron constituted more than 90 per cent of the total, and in the other, less than 50 per cent. The investigators could find no significant correlation between the hemoglobin levels and either the total intakes of iron or the intake of inorganic iron. They expressed the opinion that although the intake of iron may be a factor in regulating the hemoglobin level, other factors predominated under the conditions of their study.

The fact that animals under some conditions appeared to be unable to utilize the organic portion of the iron in their food made the question as to whether children also would be unable to utilize that portion seem worthy of investigation. The present study was begun with this idea in mind. It was felt also that a study of this type would furnish some information concerning the iron requirement of the infant, about which little was known.

## EXPERIMENTAL PROCEDURE

The subject of this experiment was a normal, healthy infant. The study of his iron metabolism was not started until he was 6 months of age, at which time it was felt that any iron stores present at birth would have been largely depleted. During the eight months of the study, there were but three interruptions. One diet proved to be constipating, and it was changed; the other two interruptions were due to slight infections of the upper respiratory tract. Each time the study was discontinued until the infant had entirely recovered. His daily life was as nearly normal as possible, and as a result he developed much the same way as would any normal child. He sat without assistance at 8 months of age and stood alone when he was 1 year old. His weight and height during the entire

3. Vahlteich, E. M.; Rose, M. S., and MacLeod, G.: Effect of Digestibility upon the Availability of Iron in Whole Wheat, J. Nutrition **11**:31 (Jan.) 1936.

4. Widdowson, E. M., and McCance, R. A.: Iron in Human Nutrition, J. Hyg. **36**:13 (March) 1936.

study were in the high normal range according to the Woodbury [5] standards from the Children's Bureau of the United States Department of Labor, 1921.

Foods were selected which for the most part are commonly used in infant feeding, and therefore the diet was comparable to that of a normal child of the same age. Five mixed formula feedings were given daily until the infant was 10 months of age, at which time he was put on four formula feedings a day. At this time feeding with a spoon was started, a cereal which contained small amounts of iron being used.[6] Gradually, as the child became accustomed to the spoon, and it was felt that feedings given with it could be as accurately measured as could bottle feedings, the major portion of his solid foods was given with a spoon. At the age of 1 year he was receiving three meals a day.

The infant took his food exceptionally well and seldom refused any. The formula bottles were rinsed with distilled water and the rinsings either given after the feeding or added to the next feeding to insure no loss. A weighed piece of gauze was placed about the child's neck at each feeding time, and any regurgitations were calculated from the gain in the weight of the gauze during the feeding. The total weight of the regurgitations was in every case much less than the experimental error incurred in the analyses of the food. Any small amounts of food which were refused were analyzed for iron.

The iron metabolism was studied for twenty-eight periods of five days each. During the first twelve periods a metabolism frame was used, and in that portion of the study the same diet was given for a period of five days when no collections were made and then for three successive five day collection periods, with intervals between them of two days when no collections were made.

When the child had reached the age of 10½ months a nursery chair with a specially constructed harness was used for the collection of feces. As a result of this, collections could be made continuously, although the stools were marked off with carmine for each five day period as had been done during previous periods. The infant was regular in his elimination, and little difficulty was encountered in training him. No collection of urine was made during the last sixteen periods, but as the amount of iron in the urine is always less than 1 per cent of the total excretion of iron, it seemed justifiable to consider it constant and make allowance for it in calculating the total excretion. Furthermore, the child was at the age when it was necessary that he be allowed to exercise freely for proper development. When the nursery chair rather than a metabolism frame was used, he could spend the greater part of the day in a play pen on the sun porch or in the play room in the company of other children. It was felt that his development under these conditions would closely approach that of any normal child.

The diets for each period as well as the amount of each food given daily are shown in table 1. As many foods as possible were obtained in quantities sufficient to last for several months to insure uniformity in quality and consequent constancy of the intake of iron. Food for each day was weighed on a platform balance and was transferred quantitatively to the bottles used for feeding the formula. Powdered milk,[7] cane sugar, orange juice, cod liver oil and a cereal were used

5. Woodbury, R. M.: Statures and Weights of Children Under Six Years of Age, Bulletin 87, U. S. Dept. of Labor, Children's Bureau.

6. Cream of Wheat was the cereal used.

7. Powdered milk was furnished, in the form of Dryco, by the Dry Milk Company.

in the diet throughout the entire study. A strained vegetable[8] also was included during all but the four periods when beef and cellulose were fed.

The general plan of the study was to note the retention of iron and the formation of hemoglobin at several levels of intake and with different proportions of inorganic and organic iron at each level. That is, a given amount of iron, with as low a percentage of iron in the inorganic form as possible, was fed for at least three periods; the same amount of iron, with a high percentage in the inorganic form, was fed for an equal number of periods. The same procedure was then

TABLE 1.—*Dietary for the Entire Study*

| Period No. | Diet | Calories | Copper Content, Mg. per Day |
|---|---|---|---|
| 1-3 | Basic diet 1*<br>20 Gm. Cream of Wheat<br>70 Gm. strained spinach | 860 | 0.22 |
| 4-6 | Basic diet 1<br>20 Gm. Cream of Wheat<br>50 Gm. strained peas | 860 | 0.26 |
| 7-9 | Basic diet 1<br>20 Gm. special Baby Ralston<br>240 Gm. strained spinach | 875 | 0.30 |
| 10-12 | Basic diet 1<br>20 Gm. special Baby Ralston<br>100 Gm. strained peas | 875 | 0.36 |
| 13-16 | Basic diet 1<br>30 Gm. Cream of Wheat<br>100 Gm. strained peas<br>Soluble ferric pyrophosphate = 1.68 mg. iron<br>Cupric sulfate = 0.09 mg. copper | 915 | 0.51 |
| 17-20 | Basic diet 1<br>30 Gm. Cream of Wheat<br>100 Gm. strained peas<br>3 Gm. VioBin | 925 | 0.49 |
| 21-22 | Basic diet 1<br>30 Gm. Cream of Wheat<br>50 Gm. strained peas | 900 | 0.28 |
| 23-26 | Basic diet 2†<br>30 Gm. Cream of Wheat<br>100 Gm. beef<br>10 Gm. cellu-flour | 920 | 0.34 |
| 27-28 | Basic diet 1<br>40 Gm. Cream of Wheat<br>150 Gm. strained peas<br>Soluble ferric pyrophosphate = 0.89 mg. iron | 970 | 0.55 |

* Basic diet 1 consisted of 115 Gm. powdered milk, 45 Gm. cane sugar, 60 cc. orange juice and 8 cc. cod liver oil.

† Basic diet 2 was the same as basic diet 1 except that the amount of powdered milk was reduced to 100 Gm.

repeated with a larger amount of iron. Only such foods were used as are generally considered suitable for the diet of other children of the same age, and the amounts fed were not above those which are given normally.

In the first six periods the total daily intake of iron was kept constant at 2.6 mg. The daily intake of inorganic iron during periods 1 to 3 was 1.9 mg. but was raised to 2.2 mg. during periods 4 to 6. This difference in the amount of inorganic iron was the result of feeding spinach in the first three periods and peas in the last three. The same cereal was given throughout the entire six periods.

8. All vegetables were supplied by the Gerber Products Company.

During periods 7 to 12 the total daily intake of iron was 3.6 mg. The daily intake of inorganic iron was 2.7 mg. in periods 7 to 9 and 3.4 mg. in periods 10 to 12. The change in the amount of inorganic iron was again the result of substituting peas for spinach. A different cereal [9] with a higher iron content was used throughout periods 7 to 12 which, with the increased amounts of vegetables, accounted for the higher level of the intake of iron.

The total daily intake of iron in periods 13 to 20 was 4.8 mg., of which 4.1 to 4.6 mg. was inorganic. The infant received peas and cereal during the entire time but in periods 13 to 16 received additional iron as soluble ferric pyrophosphate and copper as cupric sulfate. In periods 17 to 20 he was given 3 Gm. daily of a commercial wheat germ product [10] high in vitamin B, which contained the same amounts of iron and copper given as salts in the four previous periods.

In periods 21 and 22 the total daily intake of iron was reduced to 2.7 mg. by using a cereal of lower iron content and a smaller amount of peas. These periods on a lower level of intake were introduced to deplete any stores which might have been built up as a result of the higher intake of the previous periods.

After feeding this lower level for two periods, cooked ground beef was gradually introduced into the diet, until after a few days the infant was receiving 100 Gm. daily. The beef was purchased as round steak, all the fat was removed and the lean was finely ground in a meat grinder. Sufficient lean beef for the daily feeding was packed into a small pyrex beaker, the top of which was covered tightly with waxed paper. The meat was then cooked thirty minutes under steam pressure. A sample for analysis was treated similarly. During periods 23 to 26 the child received beef and a purified cellulose flour [11] but no vegetable. The amount of powdered milk received during these periods was slightly less than in previous periods because of the additional calories and protein in the meat. The total daily intake of iron during periods 23 to 26 was 5.2 mg., only 3.2 mg. of which was inorganic iron.

The total daily intake of iron in the last two periods was kept at 5.3 mg., but the intake of inorganic iron was raised to 4.6 mg. by the substitution of peas and soluble ferric pyrophosphate for the beef and cellulose flour. The amount of powdered milk was again raised to the level fed previous to period 23.

The total amount of iron in food and excreta was determined by a modification of Stugart's method,[12] which we [13] have described elsewhere. The urine was collected in glass bottles, and it was preserved with thymol and by refrigeration until the end of each five day period, when it was thoroughly mixed and measured.

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9. A special form of Baby Ralston, without the added iron and calcium salts, was furnished by the Ralston Purina Company.

10. VioBin, a stabilized, defatted product of the germ of wheat, was furnished by the VioBin Corporation.

11. The cellulose flour was purchased in the form of Cellu-Flour. Since it contained appreciable amounts of iron, the iron was removed by treating with hot hydrochloric acid. After the mixture had been filtered, the flour was washed with distilled water until the washings showed no reaction to the test for chlorides. The purified product was then analyzed for iron, and the amount received in the daily ration was added to the intake of iron in other forms.

12. Stugart, R.: Determination of Iron in Milk and Other Biological Materials, Indust. & Engin. Chem. (analyt. ed.) **3**:390 (Oct.) 1931.

13. Schlutz, F. W.; Morse, M., and Oldham, H.: The Influence of Fruit and Vegetable Feeding upon the Iron Metabolism of the Infant, J. Pediat. **3**:225 (July) 1933.

Feces were collected in porcelain dishes, and the total amount for the period was dried to constant weight and ground in a porcelain mortar. Aliquots of each food were taken every day and made into separate composites which were analyzed at the end of each period. In the case of the powdered milk, cane sugar and cereals, which were obtained in quantities, the contents of each lot were thoroughly mixed, sampled and analyzed, making it unnecessary to take daily aliquots. Care was taken to keep food from being contaminated with extraneous iron after aliquots for analyses had been taken. Distilled water was used in making up the formulas. Pyrex glassware exclusively was used for cooking purposes and analyses. Ashing was done in platinum dishes.

The amount of inorganic iron was determined by various modifications of Hill's[14] *a, a'*-dipyridine method. The earlier modifications of this method made by the Wisconsin group[15] and those made by Shackleton and McCance[16] gave similar results. Since a supply of purified sodium hydrosulfite was available, it was used as a reducing agent instead of hydroquinone. Results of analyses were more consistent when blanks were used to counteract the effect of plant pigments than when the pigments were precipitated with lead acetate before making the colorimetric comparison according to later modifications of the *a, a'*-dipyridine method made by Kohler and his associates.[17] In precipitating the plant pigments with lead acetate the resulting solution was often cloudy even after centrifugating and filtering, and a colorimetric comparison was impossible. Because of this difficulty colors were compared with those of a set of standards by using a comparator.

When changes in diet were made, a composite of foods which represented a portion of an average day's intake was weighed out, and the amount of copper in the mixed sample was determined by Daniels and Wright's[18] modification of McFarlane's[19] method. No attempt was made to analyze the excreta to determine the amount of copper present.

The amount of hemoglobin was determined weekly by the Newcomer method.

Nitrogen balances were ascertained every third period during the first twelve periods. The child showed a strongly positive nitrogen balance during these periods. As he was gaining in weight regularly, it was felt that to determine the nitrogen balances in the later periods would be of no significant value in this study.

## COMMENT ON RESULTS

Both the total intake of iron and the intake of inorganic iron as well as the corresponding retention and the values of hemoglobin for the twenty-eight periods are shown in the chart. Results of the analyses of food and excreta are listed in tables 2 and 3.

14. Hill, R.: A Method for the Estimation of Iron in Biological Material, Proc. Roy. Soc., London, s.B **107**:205 (Nov.) 1930.

15. Elvehjem, Hart and Sherman.[15a] Sherman, Elvehjem and Hart.[15b]

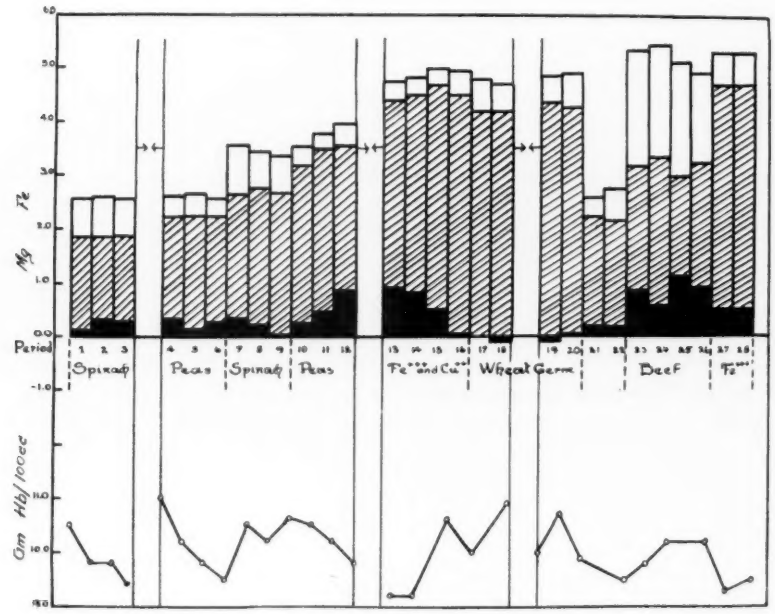
16. Shackleton, L., and McCance, R. A.: The Ionisable Iron in Foods, Biochem. J. **30**:582 (April) 1936.

17. Kohler, G. O.; Elvehjem, C. A., and Hart, E. B.: Modifications of the Bipyridine Method for Available Iron, J. Biol. Chem. **113**:49 (Feb.) 1936.

18. Wright, O. E.: Personal communication.

19. McFarlane, W. D.: Application of the Sodium Diecthyldithiocarbamate Reaction to the Micro-Colorimetric Determination of Copper in Organic Substances, Biochem. J. **26**:1022 (June) 1932.

The irregularity of the retentions as measured in the first twelve periods made it difficult to determine the availability of the organic iron of vegetables. The results are therefore somewhat ambiguous. In the first six periods, with the total daily intake of iron at 2.6 mg., it made no difference whether the intake of inorganic iron was 1.9 mg., as in periods 1 to 3, or 2.2 mg., as in periods 4 to 6. The average retentions were 0.24 mg. for the first three periods and 0.25 mg. for the next three periods, and they paralleled the total intake of iron rather than the intake of inorganic iron. On the other hand, in periods 7 to 12, with a higher total intake of iron (3.6 mg.), the retention was higher




The total intake of iron for each period is represented by the entire column; the intake of inorganic iron, by the cross-hatched portion of the column, and the retention of iron, by the black portion. The values of hemoglobin also are shown. The arrows indicate the intervals during which the study was interrupted.

in the last three periods, coincidentally with a higher intake of inorganic iron.

Whether this higher retention was actually related to the higher intake of inorganic iron, or to the higher total intake of iron which took place during the last two periods on account of the higher iron content of the peas and the orange juice given at that time, is open to question. The fact that the retention in period 10 was comparable to those in preceding periods, although the intake of inorganic iron was decidedly

higher, again made it seem that the percentage of inorganic iron in the intake does not influence the retention. When represented graphically, either as total iron or on a milligram per kilogram basis, the trend of the retention seemed to follow that of the total intake of iron more

TABLE 2.—*Total Intake of Iron, Intake of Inorganic Iron, Total Output of Iron and Corresponding Retention*

| Period No. | Total Intake of Iron, Mg. per Day | Intake of Inorganic Iron, Mg. per Day | Intake of Inorganic Iron, Percentage of Total Intake | Total Output of Iron, Mg. per Day | Retention of Iron, Mg. per Day |
|---|---|---|---|---|---|
| 1 | 2.58 | 1.85 | 72 | 2.45 | +0.13 |
| 2 | 2.60 | 1.84 | 71 | 2.29 | +0.31 |
| 3 | 2.56 | 1.87 | 73 | 2.27 | +0.29 |
| 4 | 2.61 | 2.21 | 85 | 2.28 | +0.33 |
| 5 | 2.66 | 2.22 | 83 | 2.52 | +0.14 |
| 6 | 2.52 | 2.22 | 88 | 2.25 | +0.27 |
| 7 | 3.55 | 2.62 | 74 | 3.22 | +0.33 |
| 8 | 3.41 | 2.74 | 80 | 3.20 | +0.21 |
| 9 | 3.35 | 2.63 | 78 | 3.33 | +0.02 |
| 10 | 3.53 | 3.18 | 90 | 3.29 | +0.24 |
| 11 | 3.79 | 3.48 | 92 | 3.32 | +0.47 |
| 12 | 3.98 | 3.53 | 89 | 3.14 | +0.84 |
| 13 | 4.71 | 4.38 | 93 | 3.81 | +0.90 |
| 14 | 4.80 | 4.45 | 93 | 3.99 | +0.81 |
| 15 | 4.97 | 4.66 | 94 | 4.46 | +0.51 |
| 16 | 4.90 | 4.44 | 91 | 4.85 | +0.05 |
| 17 | 4.76 | 4.16 | 87 | 4.75 | +0.01 |
| 18 | 4.68 | 4.18 | 89 | 4.79 | −0.11 |
| 19 | 4.81 | 4.32 | 90 | 4.91 | −0.10 |
| 20 | 4.89 | 4.22 | 86 | 4.82 | +0.07 |
| 21 | 2.59 | 2.22 | 86 | 2.38 | +0.21 |
| 22 | 2.75 | 2.15 | 78 | 2.57 | +0.18 |
| 23 | 5.29 | 3.17 | 60 | 4.44 | +0.85 |
| 24 | 5.38 | 3.31 | 62 | 4.80 | +0.58 |
| 25 | 5.05 | 2.98 | 59 | 3.93 | +1.12 |
| 26 | 4.86 | 3.22 | 66 | 3.95 | +0.91 |
| 27 | 5.22 | 4.63 | 89 | 4.71 | +0.51 |
| 28 | 5.22 | 4.63 | 89 | 4.71 | +0.51 |

TABLE 3.—*Total and Inorganic Iron Content of Various Foods*

| Food | Total Iron, Mg. per 100 Gm. | Range in Samples Analyzed | Inorganic Iron, Mg. per 100 Gm. | Range in Samples Analyzed | Number of Lots Analyzed | Inorganic Iron, Percentage |
|---|---|---|---|---|---|---|
| Powdered milk | 1.30 | (1.12-1.65) | 1.21 | (0.99-1.64) | 3 | 93 |
| Orange juice | 0.52 | (0.31-0.80) | 0.52 | (0.31-0.80) | 28 | 100 |
| Strained peas | 1.40 | (1.20-1.70) | 1.30 | (0.84-1.62) | 18 | 93 |
| Strained spinach | 0.90 | (0.72-1.02) | 0.50 | (0.44-0.56) | 6 | 56 |
| Cream of Wheat | 0.61 | (0.57-0.67) | 0.50 | (0.50-0.50) | 3 | 82 |
| Special Baby Ralston | 3.29 | ..... | 3.20 | ..... | 1 | 97 |
| Beef (ground and cooked) | 2.83 | (2.52-3.05) | 0.88 | (0.70-0.95) | 4 | 31 |
| VioBin | 58.50 | ..... | 53.80 | ..... | 1 | 92 |

closely than the intake of inorganic iron. However, the fact that the retention in periods 7 to 9 was slightly lower than that in periods 1 to 6, whereas the total intake of iron was higher, also indicates that retentions do not always follow the total intake of iron.

A wavelike trend, similar to that found by Porter-Levin [20] in her studies of retention of calcium and phosphorus, may be noticed throughout this entire study. If only the total iron is considered, a tendency toward increased retentions with higher intakes is seen. For instance, the average retention in periods 1 to 6, with the total intake of iron at 2.6 mg., was 0.25 mg., whereas the average retention during periods 7 to 12, with the total intake of iron at 3.6 mg. was 0.35 mg.

The amount of hemoglobin fell during the first six periods but tended to show slighly higher values during periods 7 to 12 when the total intake of iron was higher. No differences were noted which could be attributed in any way to the inorganic iron content of the diet. However, since almost 80 per cent of the values of hemoglobin for the entire study lay between 9.7 and 10.7 Gm. per hundred cubic centimeters of blood, it was felt that no significance could be attached to results showing such slight variation.

This lack of significant change in the hemoglobin content of the blood is not surprising when the rapidly changing volume of the blood is considered. During the period of the study the subject gained 4.8 Kg. in weight. For an infant of his age, the gain in weight would correspond to a gain of 370 cc. in the blood volume if MacIntosh's [21] figure of 77 cc. of blood per kilogram of body weight were used and an even greater gain if the larger figure of 86 cc., as reported by Darrow and his colleagues [22] were used. This would represent an increase of 37 Gm. of total circulating hemoglobin in the case of the infant studied, as the average hemoglobin content of his blood was 10 Gm. per hundred cubic centimeters. Since the hemoglobin molecule contains 0.34 per cent of iron, the gain in hemoglobin would mean an increase of 126 mg. in the total amount of circulating iron. The total amount of iron retained during the 28 periods was 56.9 mg., or an average of 0.41 mg. daily. Assuming that the infant stored iron at this average rate for the entire time of the study (two hundred and thirty-eight days), the total storage would have been only 96.6 mg. This is less than the amount needed for the computed increase in hemoglobin, and it is evident that under these conditions a higher concentration of hemoglobin in the blood could not have been expected.

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20. Porter-Levin, T.: Calcium and Phosphorus Metabolism of Normal Preschool Children: Successive Balance Studies Showing the Range of Variation in Calcium and Phosphorus Storage, J. Am. Dietet. A. **9**:22 (May) 1933.

21. MacIntosh, R.: The Determination of the Circulating Blood Volume in Infants by the Carbon Monoxide Method, J. Clin. Investigation **7**:203 (June) 1929.

22. Darrow, D. C.; Soule, H. C., and Buckman, T. E.: Blood Volume in Normal Infants and Children, J. Clin. Investigation **5**:243 (Feb.) 1928.

There is no conclusive evidence, then, in either the retentions of the values of hemoglobin found during the first twelve periods, that this child could utilize the iron of peas, which is 93 per cent inorganic iron, better than the iron of spinach, which is only 56 per cent inorganic iron.

It would have been preferable to have a more pronounced difference in the levels of inorganic iron, but this was impossible on account of the fact than in practically all foods suitable for use in the diets of infants 90 to 100 per cent of the iron is in the inorganic form. A large number of strained fruits and vegetables and refined cereals were analyzed, and spinach alone was found to contain appreciable amounts of iron that did not react with the $\alpha,\alpha$-dipyridine. Results on spinach consistently showed that about 56 per cent of its iron was in the ionizable form. This is a somewhat higher proportion than was found by Elvehjem and his co-workers,[23] but it agrees well with the results of Shackleton and McCance.[16] The difference between results from various laboratories may be due to the different varieties of spinach used, although the fact that fresh material was analyzed in some cases and a cooked, strained product in others would undoubtedly influence the results.

During periods 13 to 20, the availability of iron as an inorganic iron salt, soluble ferric pyrophosphate, was compared with that of the iron in a commercial wheat germ product, the total iron content of which had been shown by analyses to be practically all in the inorganic form. Both the total intake of iron and the intake of inorganic iron were kept as constant as possible throughout these eight periods. The average daily retention was +0.57 mg. for periods 13 to 16, with an average total intake of 4.8 mg. of iron, 92 per cent of which was inorganic, as compared to an average daily retention of —0.04 mg. for periods 17 to 20, with an average total intake of 4.8 mg. of iron, 88 per cent of which was inorganic. The values of the hemoglobin during this time tended to remain at a higer level despite the negative balances in periods 18 and 19.

The definite lowering of the retention when the wheat germ product was given suggests the possibility that it was influenced by the increased vitamin B content of the diet. This same effect on the iron balance was noticed by us [13] when an extract of vitamin B was given to an anemic child. The child, who had had a strongly positive iron balance, stored little iron while the vitamin was added to the diet. There was no noticeable change in the consistency or frequency of the stools in either case. The additional vitamin given to the subject of this study

23. Elvehjem, Hart and Sherman.[18a] Sherman, Elvehjem and Hart.[18b] Kohler, Elvehjem and Hart.[17]

amounted to only 26 international units [24] daily, which is not considered excessive for a child of his age. The fact that low retention occurred during period 16, before the feeding of wheat germ was begun, suggests another possible explanation. It is possible that period 16 marked the beginning of a series of low retentions and that on this level of intake such retentions would have continued, regardless of the type of food given. A further investigation is being planned in regard to the effect on the iron balance of the addition of small amounts of vitamin B to a normal diet.

It will be noted in the chart that the study was interrupted between periods 18 and 19, during the time that the wheat germ product was given. This interruption was due to a slight infection of the upper respiratory tract. The study was discontinued at the onset of the infection and was not resumed until the child had recovered completely. A similar interruption occurred between periods 12 and 13, and since exceptionally high retentions were found in that instance, it does not seem probable that the low retentions in periods 17 to 20 could be related in any way to the infection.

In periods 21 and 22, when the intake was reduced to the initial low level of 2.6 mg. per day, the retention was +0.20 mg., closely approximating the retention with a similar intake during periods 1 to 6, when the child was much younger. However, when beef was introduced into the diet, which almost doubled the total intake of iron while it raised the intake of inorganic iron only 45 per cent, the retention of iron was consistently higher than it had been at any previous time on similar intakes. During periods 23 to 26 the average daily retention was +0.87 mg., as compared to +0.57 mg. during periods 13 to 16. The values of hemoglobin, however, showed no gain during these periods.

In periods 27 and 28, although the total intake of iron was kept at the same level of approximately 5 mg., the inorganic iron constituted 89 per cent of the total, as compared to 62 per cent during the four periods just previous. The average retention was only +0.51 mg., and the hemoglobin continued to be low. The retentions shown for the last two periods are in reality those for one period of ten days. It was represented on the chart as two periods because the time involved was double that of any other period. Difficulty was encountered in separating the feces for the two periods, and it was considered best to present average results. During the last few days of period 28 the weather was very warm, and parts of feedings were refused. However, the total amount refused did not appreciably affect the intake, and it would seem that the drop in retention was of significance, since the average

24. Dr. Elizabeth Knott determined the vitamin B content of VioBin by rat assay, using standard technic.

daily retention (+0.51 mg.) was nearly the same as that in periods 13 to 16 (+0.57 mg.), when the child was receiving a similar diet and intake.

The higher retentions which were found when beef was fed certainly show that the child could utilize the iron of beef, of which a low percentage is inorganic. The fact that retentions during periods 23 to 26 were higher than in any of six other periods in which the total intake of iron was approximately the same while the intake of inorganic iron was much higher makes it quite conclusive.

The intake of copper did not vary appreciably in the periods under comparison, as is shown in table 1. In periods 27 to 28 it was higher than in the two groups of periods which preceded them, but the higher level seemed to have no beneficial influence on the hemoglobin.

The intake of iron (0.3 to 0.4 mg. per kilogram) in the early part of the study was low as compared to the requirement of preschool children of 0.5 to 0.6 mg. per kilogram as recommended by Rose and her associates,[25] Leichsenring and Flor [26] and Daniels and Wright.[27] However, Elvehjem and his collaborators [1c] considered it necessary that subminimal amounts of iron be fed if the availability of the iron is under consideration. Accordingly, in the first twelve periods the intake was as low as seemed advisable when the health of the child was taken into consideration. In the later periods, the intake nearly reached the optimum on the basis of milligram per kilogram requirements for preschool children. While the infant in this study had a positive iron balance at all times, with the exception of two of the periods in which wheat germ was fed, the total retentions as well as the retentions per kilogram increased markedly on the higher intakes. Since the retentions were still increasing when the study came to an end and since the hemoglobin remained practically constant, it is quite evident that the child was receiving no more than his maintenance requirement of iron. Since the intake during the latter part of the study equaled the standard set for preschool children, it is quite probable that the optimum intake of iron for children of this age on a milligram per kilogram basis is higher than that for older children. This could be accounted for by the more rapid change both in weight and in the volume of the blood at the younger age. Needless to say, studies of other subjects, with higher intakes, are necessary before any definite suggestions can be made.

25. Rose, M. S.: Vahlteich, E. M.; Robb, E., and Bloomfield, E. M.: Iron Requirement in Early Childhood, J. Nutrition **3**:229 (Nov.) 1930.

26. Leichsenring, J. M., and Flor, I. H.: The Iron Requirement of the Preschool Child, J. Nutrition **5**:141 (March) 1932.

27. Daniels, A. L., and Wright, O. E.: Iron and Copper Retentions in Young Children, J. Nutrition **8**:125 (Aug.) 1934.

SUMMARY

In this study the availability of inorganic and organic iron from different sources was determined by studying the retention of iron in a normal child.

With a low level of intake no difference was found in the retention when the inorganic iron of the diet was increased, the total intake of iron remaining constant. With a slightly higher level, higher retentions were found in two of three periods when the inorganic iron was increased. However, the total amount of iron was also higher in the periods of increased retention. Therefore, no conclusive evidence was obtained that only the inorganic iron was utilized.

Retentions were found to be much higher with a diet which contained iron and copper salts than with one which contained the same amount of iron and copper in the form of a wheat germ product. The amount of inorganic iron was approximately the same in the two diets, showing that some other factor was present. It is suggested that this factor may be the vitamin B in the wheat germ.

With a diet containing cooked beef which was low in inorganic iron, the retention of iron was consistently higher than with other diets which contained the same amounts of total iron and much larger amounts of inorganic iron. The iron of beef, of which a large portion is organic, was well utilized.

The data, therefore, indicate that in the case of the subject studied the availability of the iron in the food could not be determined by its reaction to $\alpha,\alpha$-dipyridine.

It is suggested that the optimal requirement of iron for a child less than 1 year of age is more than 0.5 mg. per kilogram.

Helpful criticism was given and suggestions were made by Dr. Lydia J. Roberts of the Department of Home Economics of the University of Chicago.

# THE FOUR LEAD ELECTROCARDIOGRAM OF CHILDREN

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Recent years have brought increasing interest in the use of the electrocardiogram as a means of understanding the damage to the heart muscle wrought by disease. Since Einthoven's discovery of the string galvanometer, this instrument has been used in the study of the direction, amplitude and time relations of the electrical currents produced by the contraction of the heart muscle. For over sixty years this was done only as a scientific procedure, with little clinical application. In recent years, however, more and more interest has been focused on the clinical value of such a study, until its merit has become definitely established. Three standard leads have been used, and these have yielded a great deal of information. However, it was thought that still more information could be gained if the technic was modified. Wolferth and Wood [1] in 1932 reintroduced and made popular a fourth lead, or so-called chest lead. This modification of technic was thought to elicit information as to damage in parts of the myocardium which were "silent" to the conventional leads.

They studied serially two patients with coronary disease. In their first case the conventional electrocardiogram yielded no diagnostic information until the fourth day, while the fourth lead showed changes on the first day. In their other case the findings were parallel, but more striking in lead IV. They concluded that the fourth lead aided materially in the diagnosis in certain cases of myocardial infarction.

After their work, numerous investigators adopted the use of the chest lead and reported their findings. Levine and Levine [2] pointed out that in 11 per cent of his cases of angina pectoris evidence of myocardial damage could be demonstrated with the chest lead when it was

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From the Department of Pediatrics, University of Minnesota, and the Lymanhurst Health Center and Convalescent Cardiac Home.

1. Wolferth, C. C., and Wood, F. C.: The Electrocardiographic Diagnosis of Coronary Occlusion by the Use of Chest Leads, Am. J. M. Sc. **183**:30, 1932.

2. Levine, H. D., and Levine, S. A.: An Electrocardiographic Study of Lead IV with Special Reference to the Findings in Angina Pectoris, Am. J. M. Sc. **191**:98, 1936.

missed with the conventional leads. Hoffman and Delong [3] verified the value of the chest lead in their series of cases. They observed that the findings in the chest lead did not always parallel those in the conventional lead. They expressed the opinion that since pathologic changes are not all recorded in either the chest lead or the routine leads alone it is worth while to obtain four leads in all cases of suspected or proved myocardial damage. Katz and Kissin [4] stated that lead IV should be taken as a matter of routine in all cases of suspected or recent coronary occlusion.

The aforementioned papers all dealt primarily with forms of heart disease in adults. As has been recognized, electrocardiographic study is especially valuable in cases of myocardial damage due to coronary disease. Its use with children has been more limited, and results have frequently been disappointing. Consequently, we were interested in determining what additional aid we could obtain by use of the fourth lead with children. If such a procedure could give us additional diagnostic information in an appreciable number of cases, we felt that it should be adopted.

Perusal of the literature showed us that a standard technic had been fairly well adopted. The right arm electrode was placed on the anterior part of the chest just to the left of the sternum, with its center approximately in the fourth interspace. The left arm electrode was placed at a corresponding level on the back, to the left of the spine. Bohning and Katz [5] tabulated the criteria for the normal lead IV and abnormal variations in lead IV of adults. These criteria are given in table 1. The evidences of normal and of abnormal conduction were the same in the fourth lead as in the conventional leads.

No comparable table was found for children, but we found numerous articles in which it was claimed that deflections which are considered abnormal in the electrocardiograms of adults are normal in those of children. The greatest discrepancy seemed to be in the direction of the P wave and of the T wave. The electrocardiograms of normal adults have a negative, or diphasic, P wave, while those of children may have a negative, diphasic or positive P wave. Robinow, Katz and Bohning [6]

3. Hoffman, A. M., and Delong, E.: Standardization of Chest Leads and Their Value in Coronary Thrombosis and Myocardial Damage, Arch. Int. Med. **51**:945 (June) 1933.

4. Katz, L. N., and Kissin, M.: A Study of Lead IV, Am. Heart J. **8**:595, 1933.

5. Bohning, A., and Katz, L. N.: Four-Lead Electrocardiography in Coronary Sclerosis: A Study of a Series of Consecutive Patients, Am. J. M. Sc. **189**:833, 1935.

6. Robinow, M.; Katz, L. N., and Bohning, A.: The Appearance of the T-Wave in Lead IV in Normal Children and in Children with Rheumatic Heart Disease, Am. Heart J. **12**:88, 1936.

found that the P wave in lead IV of children appeared to have the same range of contour as that in lead IV of adults, except that upright P waves were more common for children. No significant deviation in $P_4$ was noted by them when they compared rheumatic children with normal children.

A similar situation was found regarding the T wave. Rosenblum and Sampson [7] found that 64 per cent of the tracings of fifty normal children showed an upright T wave. Heard, Burkley and Schaefer [8] in

TABLE 1.—*Criteria for Normal Lead IV and Abnormal Variations in Lead IV in Adults (Bohning and Katz)*

| Record | P Wave | Q Wave or Primary Negative Portion of QRS Complex | Direction of Main Deflection of QRS Complex | ST Segment | T Wave |
|---|---|---|---|---|---|
| Normal | Negative or diphasic | Always present and usually deep | Diphasic or essentially so (first deflection negative) | Occasionally isoelectric, but usually negative (less than 2 mm.) | Negative (less than 8 mm.) |
| Abnormal | 1. Isoelectric | 1. Very small | 1. Entirely positive (monophasic) | 1. Negative (2 mm. or more) | 1. Deeply negative, 8 mm. or more |
| | 2. Positive | 2. Absent | 2. Mainly positive (diphasic) with small negative first deflection | 2. Positive of any degree | 2. Barely discernible or flat and iso-electric |
| | 3. Polyphasic | | 3. Mainly positive (diphasic) with small negative deflection | | 3. Positive |
| | | | 4. Entirely negative (monophasic) | | 4. Diphasic, with first phase negative |
| | | | 5. Mainly negative (diphasic) with small positive end deflection | | 5. Diphasic, with first phase positive |
| | | | 6. Mainly negative (diphasic) with small positive first deflection | | 6. Polyphasic |
| | | | 7. Triphasic W or M types | | |
| | | | 8. Polyphasic | | |
| | | | 9. Unusually large | | |
| | | | 10. Unusually small | | |

their study of eleven fetuses through the medium of direct leads showed that a positive deflection of $T_4$ predominated. Levy and Bruenn [9]

7. Rosenblum, H., and Sampson, J. J.: A Study of Lead IV of the Electrocardiogram in Children with Special Reference to the Direction of Excursion of the T-Wave, Am. Heart J. **11**:49, 1936.

8. Heard, J. D.; Burkley, G. G., and Schaefer, C. R.: Electrocardiograms Derived from Eleven Fetuses Through the Medium of Direct Leads, Am. Heart J. **11**:41, 1936.

9. Levy, R. L., and Bruenn, H. G.: Lead IV of the Electrocardiogram in Rheumatic Fever, Proc. Soc. Exper. Biol. & Med. **32**:559, 1934; The Precordial Lead of the Electrocardiogram (Lead IV) as an Aid in the Recognition of Active Carditis in Rheumatic Fever, Am. Heart J. **10**:881, 1935.

expressed the belief that a negative T wave in the tracings of children is normal and that it tends to become positive with continued or renewed rheumatic activity. Robinow, Katz and Bohning [6] stated that a positive T wave is a normal finding for children but that the electrocardiograms of rheumatic children tend to have a higher percentage of positive T waves than those of normal children. They agreed with Levy and Bruenn that the T wave tends to become upright as the disease process becomes more aggravated. They stated that with the child, in contrast to the adult, the contour of the T wave in lead IV in a single record is apparently of no diagnostic value.

We have tabulated what we believe to be the normal and the abnormal findings for lead IV of children, so that they can be compared with those for adults (table 2).

TABLE 2.—*Criteria for Normal Lead IV and Abnormal Variations in Lead IV in Children* *

| Complex | P Wave | Q Wave | Direction of Main Deflection of QRS Complex | ST Segment | T Wave |
|---|---|---|---|---|---|
| Normal | Positive<br>Negative<br>Diphasic | Always present and usually deep | Diphasic or essentially so (first deflection negative) | Occasionally isoelectric but usually negative (less than—2 mm.) | Positive<br>Negative<br>Diphasic |
| Abnormal | 1. Tall | 1. Very small | 1. Prolonged span | 1. Deviations of more than —2 | 1. Deeply negative (8 mm. or more) |
| | 2. Broad | 2. Absent | 2. Marked notching | 2. Positive of any degree | 2. Strongly positive (8 mm.or more) |
| | | | 3. Triphasic | | |
| | | | 4. Monophasic (positive or negative) | | |

* Adapted from Bohning and Katz' table for adults and applied to children.

Levy and Bruenn [9] stressed the importance of serial studies and concluded that "in rheumatic fever the use of Lead IV is of clinical value as an aid in the recognition of active myocardial involvement and in following its course." Robinow, Katz and Bohning,[6] on the other hand, concluded that the practical value of lead IV in cases of children suffering from rheumatic heart disease is definitely limited.

If the chest lead should prove worthless for use with children, it would be best to drop it. However, it is interesting for one to conjecture why a procedure that has proved valuable in cases of coronary disease, with its resultant myocardial damage, should prove worthless in cases of myocardial damage of rheumatic origin. From the location of the electrodes on the chest, it would seem that one is obtaining curves which are more sensitive to damage in the ventricles than in the auricles. One might suspect that the myocardial damage in rheumatic heart dis-

ease is limited to the auricles. But this is not the case, for Bell [10] has shown that the entire heart muscle is involved. We are interested in this subject because the most important problem in the management of the patient with rheumatic fever is the recognition of active cardiac involvement.

We have been intrigued by the thought that the fourth lead might give aid when the conventional leads seemed to fail. We have studied this problem with our series in an attempt to establish the positive or negative value of the lead. We have been concerned entirely with children, our subjects being patients that were referred to the Lyman-

TABLE 3.—*Cases in Which the Conventional Leads Were Abnormal and Lead IV Normal* *

| Cases | Conventional Leads | Lead IV |
|---|---|---|
| Case 1 | Broad notched $P_1$<br>Delay in auriculoventricular conduction (0.22 second)<br>Swift lead | Normal |
| Case 2 | Right axis deviation<br>Broad, notched $P_1$ and $P_2$<br>Delay in auriculoventricular conduction (0.24 second)<br>Negative $T_1$, $T_2$ and $T_3$ | Normal |
| Case 3 | Delay in auriculoventricular conduction (0.24 second) | Normal |
| Case 4 | Swift lead<br>Left axis deviation | Normal |
| Case 5 | Swift lead | Normal |
| Case 6 | Swift lead | Normal |
| Case 7 | Swift lead | Normal |
| Case 8 | Swift lead | Normal |
| Case 9 | Swift lead<br>Swift lead | Normal |
| Case 10 | Right axis deviation<br>Premature ventricular beats | Normal |

* Lead IV showed the same figures on conduction as the conventional lead did.

hurst Health Center. Our study consisted of four distinct parts. First, we took seventy-two single four lead tracings for children with rheumatic heart disease and compared them with seventy-two tracings for children with no heart disease. Second, we took a series of patients with congenital heart disease to see what they would show in a four lead study. Third, we compared eight tracings obtained by the technic previously described with eight tracings taken with the left arm electrode on the left leg instead of on the left side of the back. Fourth, we ran a daily serial study of four patients with severe active rheumatic heart disease.

Our first problem was an analysis of our seventy-two four lead tracings of the children with rheumatic heart disease. It should be

10. Bell, E. T.: A Text Book of Pathology, ed. 2, Philadelphia, Lea & Febiger, 1934.

pointed out that the condition was subacute and the children convalescent. The incidence of valvulitis and crippling carditis was low. We were primarily interested in finding out whether the use of four lead electrocardiograms would give us more information regarding myocardial involvement than the use of the conventional three leads alone. Tables 3, 4 and 5 show our findings in each case in which there was an abnormal tracing.

Table 3 shows that in eight of ten of the cases the lead was what has been called a Swift lead. This finding was first described by Swift and Cohn [11] and Shapiro.[12] In this lead the ST interval is absent and there is a sharp rise from the S wave to the top of a high T wave. They expressed the belief that it was indicative of myocardial damage.

Table 4 shows the findings in five cases in which the conventional leads were normal and the fourth lead abnormal. The most constant

TABLE 4.—*Cases in Which the Conventional Leads Were Normal and Lead IV Abnormal*

| Cases | Conventional Leads | Lead IV |
|---|---|---|
| Case 1 | Normal | Positive monophasic $QRS_4$ |
| Case 2 | Normal | Positive monophasic $QRS_4$ |
| Case 3 | Normal | Negative monophasic $QRS_4$ Tall positive $T_4$, 14 mm. |
| Case 4 | Normal | Positive monophasic $QRS_4$ |
| Case 5 | Normal | Deep negative $T_4$, 10 mm. |

finding was a monophasic QRS complex in lead IV. This is the important group in our series because these are the cases in which the condition would have been missed if no fourth lead had been taken.

Table 5 shows the findings in eleven cases in which both the conventional leads and the fourth lead were abnormal. Detailed study shows what our abnormal findings in the conventional leads were and with what characteristics in lead IV they were associated. Six of the patients had Swift leads alone or associated with other abnormalities. This gives a numerical incidence of fourteen Swift leads in seventy-two cases, or a frequency of 19 per cent. In three cases in this group Swift leads were observed, the ST wave was absent from lead IV and there was a sharp drop from the S wave to a deep negative T wave. This is the mirror image of the Swift lead in the conventional tracings.

11. Cohn, A. E., and Swift, H. F.: Electrocardiographic Evidence of Myocardial Involvement in Rheumatic Fever, J. Exper. Med. **39**:1, 1924.

12. Shapiro, M. J.: Electrocardiographic Changes in Quiescent Rheumatic Disease in Children and Young Adults, Am. Heart J. **5**:504, 1930.

Table 6 presents a summary of our findings. In 7 per cent of our cases lead IV showed abnormalities which were missed with the conventional leads. By means of four lead electrocardiograms we were able to demonstrate myocardial damage in 36 per cent of our patients instead

TABLE 5.—*Cases in Which the Conventional Leads and Lead IV Were Abnormal*

| Cases | Conventional Leads | Lead IV |
|---|---|---|
| Case 1..... | Notched $P_1$ and $P_2$ | Deep negative $T_4$, 15 mm. |
| Case 2..... | Low potential in lead I | Positive monophasic $QRS_4$ |
| Case 3..... | Transition between flutter and auricular fibrillation | Deep negative $T_4$, 11 mm. |
| Case 4..... | Notching of $QRS_1$, $QRS_2$ and $QRS_3$<br>Delay in intraventricular conduction (0.12 second)<br>Swift lead | Negative monophasic $QRS_4$ |
| Case 5..... | Delay in anuriculoventricular conduction (0.24 second) | Positive monophasic $QRS_4$ |
| Case 6..... | Broad, notched $P_1$, $P_2$ and $P_3$<br>Swift lead | Positive monophasic $QRS_4$ |
| Case 7..... | Broad, notched $P_1$, $P_2$ and $P_3$ | Positive monophasic $QRS_4$ |
| Case 8..... | Right axis deviation<br>Delay in auriculoventricular conduction (0.24 second)<br>High, peaked, notched $P_1$ and $P_2$ | Negative monophasic $QRS_4$ |
| Case 9..... | Swift lead | $ST_4$ absent<br>Sharp drop from S to deep negative T |
| Case 10..... | Swift lead | $ST_4$ absent<br>Sharp drop from S to deep negative T |
| Case 11..... | Swift lead | $ST_4$ absent<br>Sharp drop from S to deep negative T |

TABLE 6.—*Summary of Findings*

| | | Percentage |
|---|---|---|
| (a) Cases in which the conventional leads were normal and lead IV abnormal..... | 5 | 7 |
| (b) Cases in which the conventional leads were abnormal and lead IV normal..... | 10 | 14 |
| (c) Cases in which both the conventional leads and lead IV were abnormal..... | 11 | 15 |
| (d) Cases in which both the conventional leads and lead IV were normal..... | 46 | 64 |
| Cases..... | 72 | 100 |
| Therefore: | | |
| Cases of myocardial damage detected by means of conventional electrocardiograms (c plus b)..... | 21 | 29 |
| Cases of myocardial damage detected by means of four lead electrocardiograms (a plus b plus c)..... | 26 | 36 |

of in 29 per cent, as would have been the case had only three leads been taken. It appears from this study that four lead electrocardiograms are a valuable aid to the diagnosis of myocardial damage in rheumatic heart disease. The efficiency of each lead seems to be about equal even if the findings are not parallel in every case. This conclusion tends to agree with the suggestion of Wolferth and Wood that certain areas

of the heart muscle which are "silent" in conventional leads have a definite effect on the chest leads. We repeat again that the fourth lead shows the same delays in conduction as the conventional leads.

Our second problem was the analysis of the electrocardiographic tracings, including the fourth lead, which were taken for thirty-three children with congenital heart disease. Fourteen of these children were boys; nineteen, girls. Nine had definite cyanosis of the skin and mucous membranes, as well as clubbing of the fingers. The condition of ten was diagnosed as patency of the interauricular septum, that of four as the tetrad of Fallot and that of one as congenital heart block, patent ductus arteriosus and patent interventricular septum. In five instances a diagnosis of congenital heart disease was made but the exact lesion could not be determined. In none of the thirty-three cases did the fourth lead

TABLE 7.—*Patients with Congenital Heart Disease*

| Boys | Girls | Cyanosis | Clubbing of Fingers | Roentgen Examination | Electrocardiogram: Conventional Lead | Electrocardiogram: Lead IV | Diagnosis |
|---|---|---|---|---|---|---|---|
| 14 | 19 | 9 | 9 | Increase in size.....20 | Heart Block...1 | Heart Block.1 | Patent interventricular septum .....10 |
| | | | | Typical contour.....21 | | | Patent ductus arteriosus.....11 |
| | | | | Increase in size alone... 4 | | | Congenital heart disease (type undetermined)..... 5 |
| | | | | Typical contour alone.. 5 | | | Pulmonary stenosis..... 1 |
| | | | | Increase in size and typical contour.....16 | | | Patent interauricular septum. 1 |
| | | | | | | | Tetrad of Fallot..... 4 |
| | | | | | | | Congenital heart block..... 1 |
| | | | | | | | Patent ductus arteriosus..... 1 |
| | | | | | | | Patent interventricular septum ..... 1 |

add additional information. In fact, little information was gained from the conventional three leads except in cases in which axis deviation helped somewhat in making a positive differential diagnosis as to the exact type of congenital lesion present.

It might be of interest to compare the findings in the roentgen examinations. Films were taken at a distance of 6 feet in every case. In twenty instances the heart was enlarged; in twenty-one the contour was typical of congenital heart disease; in four there was enlargement of the heart only, with no characteristic contour; in five the contour was characteristic of congenital heart disease, with no enlargement; in sixteen both the enlargement of the heart and the contour were typical of congenital heart disease, and in two the roentgen examination gave entirely negative results. Therefore, in thirty-one of thirty-three cases the roentgen examination showed some change which suggested a cardiac lesion, and in 50 per cent of the cases the roentgen picture itself confirmed the diagnosis.

Electrocardiography, including the use of the fourth lead, is of little value in the diagnosis of congenital heart disease except as confirmatory evidence. The axis deviation as well as certain changes in conduction should help in making an exact diagnosis. The roentgen examination in cases of congenital heart disease is of far more practical value. Table 7 shows the summary of our cases of congenital heart disease.

Our third problem was the comparison of the established chest lead with a suggested modification. For clarity, the standard technic for obtaining chest leads should be reviewed. The right arm electrode is placed on the anterior part of the chest just to the left of the sternum, with its center approximately in the fourth interspace. The left arm electrode is placed at a corresponding level in the back, to the left of

TABLE 8.—*Difference Between Standard Technic and Modified Technic*

| Cases | $P_4$, Mm. | $Q_4$, Mm. | $R_4$, Mm. | $QRS_4$, Total | Q/R Ratio | $ST_4$, Level | $T_4$, Mm. |
|---|---|---|---|---|---|---|---|
| 1. Chest and back..... | +1 | — 6 | +17 | 23 | 0.35 | 0 | +3 |
| Chest and leg..... | 0 | — 4 | +17 | 21 | 0.23 | 0 | +3 |
| 2. Chest and back..... | —2 | —12 | +21 | 33 | 0.57 | —1.5 | +2 |
| Chest and leg..... | —1 | — 7 | +18 | 25 | 0.38 | 0 | +3 |
| 3. Chest and back..... | —2 | — 8 | +18 | 26 | 0.44 | 0 | —3 |
| Chest and leg..... | —1 | — 6 | +20 | 26 | 0.30 | 0 | —3 |
| 4. Chest and back..... | —2 | —12 | +19 | 31 | 0.63 | 0 | —4 |
| Chest and leg..... | —2 | — 8 | +17 | 25 | 0.47 | 0 | —3 |
| 5. Chest and back..... | —2 | —16 | +20 | 36 | 0.80 | 0 | —8 |
| Chest and leg..... | —1 | — 7 | +13 | 20 | 0.53 | 0 | —4 |
| 6. Chest and back..... | —1 | —19 | +17 | 36 | 1.11 | 0 | —5 |
| Chest and leg..... | +1 | —23 | +17 | 40 | 1.35 | 0 | —7 |
| 7. Chest and back..... | —1 | —13 | +16 | 29 | 0.81 | 0 | +4 |
| Chest and leg..... | —1 | —10 | +17 | 27 | 0.59 | 0 | +4 |
| 8. Chest and back..... | —2 | —11 | +18 | 29 | 0.61 | 0 | +3 |
| Chest and leg..... | —1 | — 8 | +20 | 28 | 0.40 | 0 | +4 |

the spine. Because of the difficulties of placing an electrode on the back of a bedridden patient, a modification has been suggested whereby the left arm electrode is placed on the left leg instead. It was thought that this made no practical difference. We were interested in checking this impression.

We used both technics with eight patients whose four lead tracings were normal to determine what would happen. Table 8 shows our findings.

Analysis of table 8 shows that placing the left arm electrode on the left leg instead of on the back causes the electrocardiogram to resemble the conventional leads. Figures 1 and 2 show a comparison of the results obtained by the two technics. All complexes take on a more upright direction. The positive factors become more positive, and the negative factors, less negative. If one is going to study chest leads, then, one must use the standard technic.

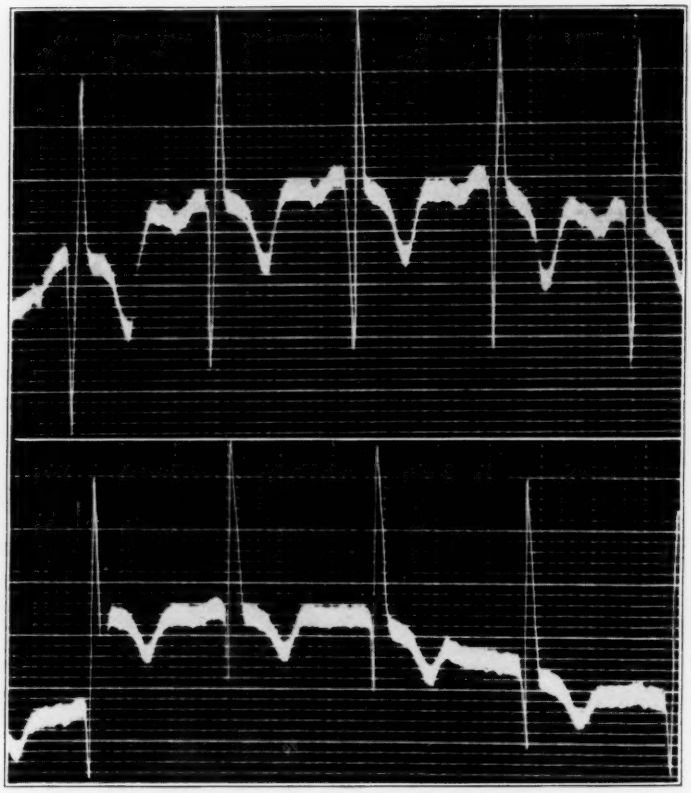

Fig. 1.—Tracings showing the difference in configuration obtained by chest and back leads (upper tracing) from that obtained by chest and leg leads (lower tracing).

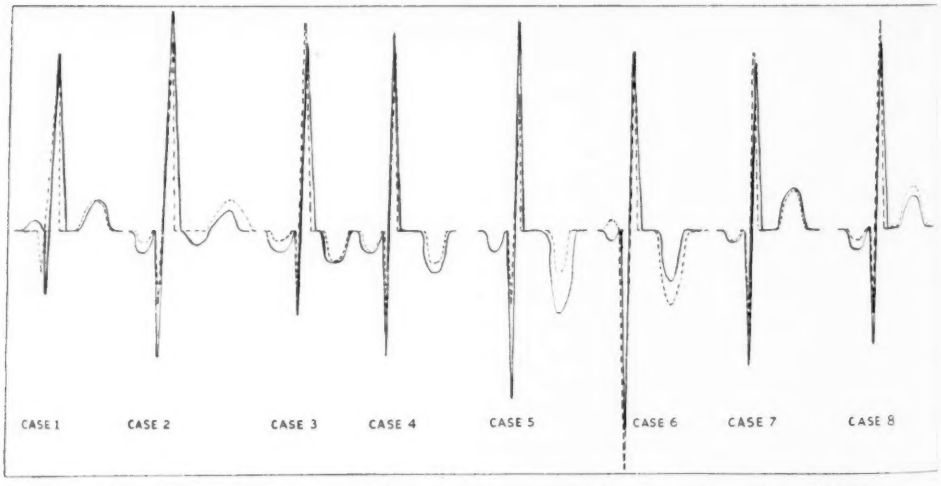


Fig. 2.—Schematic presentation of superimposed fourth leads. The solid line is that obtained by the chest and back technic. The broken line is that obtained by the chest and leg technic.

One of the most confusing things about the chest lead is the lack of standardization of technic. As a result of this confusion, many cardiologists refuse to be bothered by the new procedure. A relatively small mass of literature has accumulated, but already one finds references to the fifth, sixth, seventh and even eighth leads. This, when the chest lead has yet to prove its real merit, is distressing. If all the research done so far on modifications of the conventional leads had been done with a standard technic, one would have a wealth of material from which to draw conclusions. We wish to enter a plea for uniformity of methods.

The last portion of this paper gives the results of a serial study, with ten daily tracings, of four patients with subacute rheumatic heart disease. Our patients were children taken from the convalescent wards of the Lymanhurst Health Center. The first was a boy who showed a low voltage in lead III, a Swift type of lead II and an M form for the QRS complex. The QRS complex was mostly positive, with a $\frac{Q}{R}$ ratio of 0.35. According to Rabinow, Katz and Bohning [6] this is within the normal limits for children. They found that the average upright phase of $QRS_4$ was taller for normal children than for adults. "The $\frac{Q}{R}$ ratio (the ratio of amplitude of the negative to that of the upright phase of $QRS_4$ was therefore smaller in children than in adults." Their figures are as follows:

| | $\frac{Q}{R}$ Ratio | Range |
|---|---|---|
| Normal adults | 0.59 | |
| Normal adolescents | 0.50 | (0.3–0.6) |
| Normal children | 0.50 | (0.1–0.2) |
| Rheumatic children | | |
| (*a*) Inactive stage | 0.40 | ( 1–1.7) |
| (*b*) Acute stage | 0.40 | (0.05–2 ) |

The electrocardiograms of our patient showed a variation in $\frac{Q}{R}$ from 0.35, on the first day, to 0.17, on the tenth day. All the other findings remained the same.

There was no appreciable change in the clinical status of this patient or in that of the other three during the period of study.

In the second case there occurred a delay in the auriculoventricular conduction of 0.24 second. This was associated with an abnormally deep $T_4$. Bohning and Katz [5] placed the normal limit for the depth of $T_4$ at 8 mm. Our patient showed the following variation in $T_4$ during the ten days: 12, 10, 13, 11, 12, 9, 15, 11, 11 and 9 mm.

In the third and the fourth case, ST was persistently absent and there was a direct rise to a high T wave in leads I and II. This finding has been attributed by Swift and Cohn [11] to myocardial damage. There was no associated change in lead IV, and the ST interval was iso-electric.

Our only conclusion from this portion of our study is that in the absence of clinical changes the four lead electrocardiogram tends to be constant from day to day.

## SUMMARY

We attempt a review of the literature on four lead electrocardiograms, especially as it pertains to children.

We present our findings on single four lead tracings for seventy-two children with subacute rheumatic heart disease and for seventy-two controls.

We analyze the four lead electrocardiograms of thirty-three children with congenital heart disease.

We compare the results obtained with the standard chest leads with those obtained by placing the left arm electrode on the left leg.

We present the results of serial study, by means of daily tracings, of the four lead electrocardiograms of four children with rheumatic heart disease.

## CONCLUSIONS

1. Use of a standard technic is essential in taking fourth leads.

2. There is a definite difference between the tracings made with the standard technic and those obtained by placing the left arm electrode on the left leg. In the latter, all complexes tend to assume a more upright direction and consequently are not the same as those in the chest lead.

3. The findings in the four lead electrocardiograms seem to be constant from day to day.

4. The delays in conduction shown in the conventional leads are shown to the same degree in lead IV.

5. The fourth lead is of no help in the study of congenital heart disease.

6. The use of the conventional leads gave rise to a diagnosis of myocardial damage in 29 per cent of our cases, while the use of four lead electrocardiograms yielded this information in 36 per cent of the cases. We received diagnostic information in the fourth lead, as well as striking corroboration of the minor changes shown in the conventional leads.

# HUMAN CONVALESCENT SERUM IN THE PREVENTION AND MODIFICATION OF MEASLES

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Measles is possibly the most prevalent, the most contagious and one of the most fatal diseases of early childhood. Practically all human beings are susceptible, regardless of their age or race or the climate in which they live, but young children furnish the greatest number of cases and the highest mortality. Ninety-seven per cent of the cases occur before the age of 15 and over one-half during the first five years of life. It is difficult to prevent exposure to the disease because of its highly contagious character in the prodromal period, during which the symptoms are not diagnostic and its nature remains unrecognized. The period of highest infectivity is in the preeruptive stage. Few persons die of the disease itself, but, contrary to the popular conception, measles is a disease to be feared because of the high mortality due to complications from secondary invading organisms. The death rate from measles is highest for children under 5 years of age and especially for those under 2 years. More than 90 per cent of the deaths occur in children under 5 years old and 75 per cent in those under 2 years. It is therefore important to prevent the disease or to produce an attenuated form of it, especially during the period from infancy to the age of 6 years and in children who are in poor physical condition.

Various means of obtaining active and passive immunity have been described. A method by which active immunity can be produced was reported by Herrman [1] in 1922. He inoculated healthy infants whose mothers had a history of measles by swabbing the mucous membranes of the nose with diluted secretions taken from patients with measles from twenty-four to forty-eight hours before the appearance of the eruption. Of 165 infants inoculated, 84 had a definite rise in temperature between the eighth and the sixteenth day and showed a few spots on the face and the body. Of 75 of these children observed from four to eight years, only 5 contracted measles. None who had shown a distinct reaction

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From the Convalescent Serum Center of the Children's Hospital.

1. Herrman, C.: Arch. Pediat. **39**:607 (Sept.) 1922.

contracted the disease. However, this method does not have a wide appeal either to the laity or to the members of the medical profession.

Tunnicliff and Hoyne [2] immunized goats with green-producing diplococci and their filtrates isolated from secretions early in the course of measles and used the serum for the prevention of the disease. Ferry and Fisher [3] prepared measles toxin and antitoxin from a green-producing streptococcus, called Streptococcus morbilli, which they isolated from blood in early stages of measles, and they reported favorable results obtained by the use of the antitoxin as a prophylactic measure. Opinions differ regarding the effectiveness of these so-called specific serums in the prevention and treatment of measles, and the number of "foreign serum reactions" which result from their employment is decidedly unfavorable to their widespread use.

Since Nicolle and Conseil,[4] in 1918, first advised the injection of convalescent serum for the prevention of measles, evidence has accumulated both in Europe and in America concerning its protective value.

A. Degkwitz [5a] in 1920 and R. Degkwitz [5b] in 1921 and 1922 published the results of inoculation of more than 1,000 exposed persons with serum obtained from blood drawn between the seventh and the seventeenth day of convalescence. They reported complete protection in 85 per cent of the cases.

Von Torday [6] in 1923 summarized the results of inoculation of approximately 2,000 exposed persons and found that convalescent serum had failed to protect in less than 3 per cent of the cases.

Since that time many other articles have appeared, and all observers have been unanimous as to the good results obtained through the use of convalescent serum. Perhaps the largest series is that reported on by Park and Freeman [7] in 1926. More than 1,500 children received preventive injections, and accurate data were obtained for 979. Of these, 753 were exposed in institutions and 226 in families. In 404 of the institutional children and in all the children in families the exposure was direct. For 349 of the institutional children actual personal contact with patients with measles was not proved. Of the institutional group of

2. Tunnicliff, R., and Hoyne, A. L.: Prevention of Measles by Immune Goat Serum, J. A. M. A. **87**:2139 (Dec. 25) 1926.

3. Ferry, N. S., and Fisher, L. W.: Measles Toxin: Its Preparation and Application, J. A. M. A. **86**:932 (March 27) 1926.

4. Nicolle, C., and Conseil, E.: Bull. et mém. Soc. méd. d. hôp. de Paris **42**:336, 1918.

5. (*a*) Degkwitz, A.: Ztschr. f. Kinderh. **27**:171, 1920. (*b*) Degkwitz, R.: ibid. **25**:134 (May) 1920; Monatschr. f. Kinderh. **22**:186 (Nov.) 1921; Deutsche med. Wchnschr. **48**:26 (Jan. 5) 1922.

6. von Torday, F.: Jahrb. f. Kinderh. **102**:213 (June) 1923.

7. Park, W. H., and Freeman, R. G.: Prophylactic Use of Measles Convalescent Serum, J. A. M. A. **87**:556 (Aug. 21) 1926.

753 children, 84 per cent were completely protected and 11 per cent contracted modified measles. In the family group 52 per cent were completely protected and 42 per cent contracted modified measles. In both groups 95 per cent of the children benefited from the injections.

Debré and Ravina [8] emphasized the desirability of producing modified measles with convalescent serum rather than of attempting complete immunization. Passive immunity is of short duration, and the person is left just as susceptible to the disease as he was before; whereas modified measles, characterized by mildness and lack of complications, produces an active immunity which is probably life-long.

According to some authors (R. Degkwitz and Haas and Blum [9]), the injection of serum on or after the eighth day after exposure will not prevent or modify the disease. This statement has not been borne out in the experience of other investigators (e. g., Zingher [10] and Regan [11]), and the reason may possibly be found in variations in the amount and the potency of the serum used by different observers. Zingher (1924) stated that disease can be prevented in some patients and modified in others as late as the eighth or ninth day after exposure. Regan (1924) called attention to the type of modified measles induced by late inoculation with serum. When injected in the period of invasion, convalescent serum seemed to have a slight effect in modifying the severity of the disease, especially when given intravenously, but did not influence any of the characteristic symptoms. When serum was given late in the period of incubation, the following results were noted:

1. The period of incubation was prolonged. (In 4 instances it was prolonged to the twenty-fourth day.)
2. The period of invasion was shortened.
3. Coryza was mild or absent.
4. Koplik's spots were usually absent or atypical in evolution.
5. Enanthem was lacking.
6. Prodromal rashes occurred with greater frequency.
7. The eruption was altered, being scant or atypical, and in some instances became ecchymotic as it faded.
8. The temperature curve was distinctly lower.
9. Constitutional reactions were decidedly less pronounced.
10. Complications were practically lacking.

8. Debré, R., and Ravina, J.: Bull. et mém. Soc. méd. d. hôp. de Paris **47**:226, 1923.

9. Haas, S. V., and Blum, J.: Prophylactic Value of Blood of Convalescents in Measles, J. A. M. A. **87**:558 (Aug. 21) 1926.

10. Zingher, A.: Convalescent Whole Blood, Plasma and Serum in Prophylaxis of Measles, J. A. M. A. **82**:1180 (April 12) 1924.

11. Regan, J. C.: Symptomatology of Measles Modified by Late Serum Immunization, J. A. M. A. **83**:1763 (Nov. 29) 1924.

Regan concluded from these results that convalescent serum administered late in the period of incubation, between the sixth and the ninth day, and in a dose of from 8 to 10 cc. has the power of inducing modified measles. He stated that except in institutions and with children under 2 years of age or older patients suffering from debilitating diseases, the late inoculation of susceptible persons is far more logical than early inoculation designed to procure complete protection.

Richardson and Connor [12] attempted to produce active immunity by the injection of material containing the measles virus simultaneously with the administration of immune serum. In 2 out of 3 subjects there was no reaction. In the third a transient rise in temperature and an atypical hemorrhagic rash appeared twelve days later.

Immune adult serum (i. e., serum from adults who have had the disease in childhood) has been found to afford protection against measles, but considerably larger doses of this than of convalescent serum are required to be effective. Von Torday,[6] using adult serum in 20 cc. doses, inoculated 116 persons from the second to the sixth day after exposure and reported only 12 failures.

Barenberg and his co-workers [13] (1930) gave 30 cc. doses of adult whole blood to 56 actively exposed children; 65 per cent benefited, and complications developed in 11 per cent of the unbenefited group. In a group of 60 exposed persons who received 6 cc. each of convalescent serum, 96 per cent were protected; of these, 73 per cent escaped the disease entirely and in 23 per cent it developed in an attenuated form. There were no complications in this group.

Morales and Mandry [14] inoculated 132 children exposed by familial contact with from 20 to 40 cc. of immune adult serum; 80.3 per cent received complete protection, and in 76 per cent of those having measles it developed in an attenuated form.[14]

McKhann and Chu [15] (1933) injected placental extract intramuscularly into children susceptible to measles and secured either immunization or modification of the disease. They reported that in none of the children in this series did a local or general reaction follow the injection. Nevertheless, isolated globulins of human blood are known to produce local irritation, such as edema and erythema, and fever and malaise in

12. Richardson, D. L., and Connor, H.: Immunization Against Measles, J. A. M. A. **72**:1046 (April 12) 1919.

13. Barenberg, L. H.; Lewis, J. M., and Messer, W. H.: Measles Prophylaxis: Comparative Results, J. A. M. A. **95**:4 (July 5) 1930.

14. Morales, E. G., and Costa Mandry, O.: Relative Prophylactic Value of Convalescent and Immune Adult Measles Serums, Am. J. Dis. Child. **39**:1214 (June) 1930.

15. McKhann, C. F., and Chu, F. T.: Use of Placental Extract in Prevention and Modification of Measles, Am. J. Dis. Child. **45**:475 (March) 1933.

some subjects. McKhann [16] stated more recently that a method of preparation and administration of placental extract to eliminate reactions was under investigation.

Until active immunization can be artificially induced with the measles virus or its products, as is done with diphtheria and smallpox, convalescent serum, where it is available, will remain by far the best preventive measure against measles, both in effectiveness and in practicability.

In the past it has been difficult to obtain sufficient convalescent serum, but in places where serum centers have been established this obstacle has been obviated.

## METHOD

The Convalescent Serum Center of the Children's Hospital in Los Angeles was established Jan. 1, 1936, for the purpose of providing a continual supply of convalescent serums of proved value. The methods used in the preparation of the serums meet the specifications of the National Institute of Health.

Blood for the preparation of measles serum is drawn from fasting donors between the seventh day and the end of the second month of convalescence. It is stored in the refrigerator overnight and centrifugated for twenty minutes the following morning. After separation from the blood clot, the serum is centrifugated a second time, to remove the remaining cells. It is cultured and stored in the refrigerator for one week, pending reports of the Wassermann and the Kahn tests and the cultures. It is then pooled, recultured, filtered and, after the addition of 0.25 per cent cresol as a preservative, bottled. The greatest possible caution is taken to observe aseptic technic throughout the various steps involved in the preparation of serums, including the important process of sterilization. The sterilizers are equipped with thermometer records, which insure the maintenance of lethal temperatures, and, in addition, Diack controls are placed within the dressings and articles to be sterilized to indicate whether there is sufficient penetration of heat.

The dose of convalescent serum recommended for the prophylaxis of measles is as follows:

| | |
|---|---|
| Infants and children under 3 years | 5 cc. |
| Children over 3 years | 7.5 cc. |
| Older children and adults | 10 to 15 cc. |

This analysis is based on results obtained from the use of convalescent serum in 430 patients treated at home. The data were obtained from information cards sent to all physicians who used serum in their private practice. Five cases were only partially reported and therefore do not figure in all the tables. The purpose of the inoculation was prophylactic in 423 cases and therapeutic in 7. In all the cases in which it was prophylactic, the subject was directly exposed to measles, and in many instances, in which members of the family were already ill with the disease, the contact was intimate and prolonged.

In the entire series no reactions occurred which could be attributed to the serum.

16. McKhann, C. F.: Factors Influencing the Use of Immune Globulin (Human Placental Extract), Am. J. Dis. Child. **50**:1632 (Dec.) 1935.

PROPHYLAXIS

Of 423 exposed persons, 307, or 72.5 per cent, showed complete protection, and 106, or 25.2 per cent, had mild or modified measles; in the remaining group 5 had moderate and 5 unmodified measles (table 1).

Some idea as to the degree of mildness represented by the mild and modified form of the disease may be obtained from a summary of the remarks made by the physicians in reference to their cases of modified measles. The efficiency of the serum was "good," "excellent" or "ideal;" the disease was "modified," "greatly modified," "mild," "very mild," "atypical," "light" or "very light;" the "duration was shortened;" the "fever lasted one day, with a slight rash;" the "duration was forty-eight hours;" there was a "rapid recovery." One patient in the group had a hemorrhagic eruption, but the subsequent involvement was mild and of

TABLE 1.—*Results of Prophylaxis in 423 Exposed Persons Who Had No History of Measles*

| Age, Years | Exposed Persons | Protected | Mild or Modified Measles | Moderate Measles | Unmodified Measles | Complications | Protected, Percentage | Modified Measles, Percentage |
|---|---|---|---|---|---|---|---|---|
| 0-3 | 167 | 129 | 36 | 1 | 1 | 0 | 77.2 | 21.5 |
| 3-5 | 87 | 58 | 28 | 1 | .. | 0 | 66.6 | 32.1 |
| 5-10 | 122 | 79 | 37 | 3 | 3 | 1* | 64.7 | 31.9 |
| 10-15 | 19 | 14 | 4 | .. | 1 | 1† | 75.0 | 21.0 |
| Over 15 | 23 | 23 | .. | .. | .. | 0 | 100.0 | .... |
| Not stated | 5 | 4 | 1 | .. | .. | .. | 80.0 | 20.0 |
| Total | 423 | 307 | 106 | 5 | 5 | | 72.5 | 25.2 |

Total benefited, 97.7 per cent

* Scarlet fever simultaneously.
† Mild encephalitis.

short duration. Another child was reexposed twelve days after the administration of serum, and modified measles developed fourteen days after the reexposure. In several patients the period of incubation was prolonged, the greatest duration being twenty-three days. No patient experienced any complications.

The number of exposed persons who benefited from the administration of measles serum includes those who were completely protected from the disease and those in whom modified measles developed, making a total of 413, or 97.7 per cent.

The patients who had moderate attacks were, perhaps, wrongly omitted from the benefited group, since there is no way of knowing how severe the disease might have been if serum had not been administered. None of those with moderate attacks had complications.

The failures reported, that is, the cases of unmodified measles, which were after all relatively few, are difficult to analyze. In 1 instance the length of exposure, which occurred at school, was unknown and scarlet

fever developed coincidentally with the measles. With such a combination contributing to the severity of the illness, it is difficult to estimate the efficacy of the serum, but the fact that recovery took place without further complication speaks in its favor. The second child, aged 2 years, had congenital heart disease and contracted bronchopneumonia two weeks prior to the onset of measles. The third, a girl aged 12 years, thirteen days after the injection of serum contracted severe measles, with mild encephalitis. What the outcome without serum therapy would have been, of course, is unknown. In the remaining two patients there were no complicating factors. One was given less than the dose recommended according to age on the seventh day of exposure. The other received the amount of serum which is advised for prophylaxis if given early in the period of incubation, but she received it as late as four days before the appearance of the rash, or about the time of onset of the prodromal period in the average case. This proves nothing, however,

TABLE 2.—*Results of Prophylaxis in Relation to the Doses of Serum*

| Amount of Serum, Cc. | Exposed Persons | Modified Measles | Moderate Measles | Unmodified Measles | Modified Measles, Percentage | Protected Percentage | Modified Measles and Protected, Percentage |
|---|---|---|---|---|---|---|---|
| 2.5-4 | 27 | 11 | 0 | 0 | 40.7 | 59.3 | 100.0 |
| 5 | 219 | 54 | 3 | 2 | 24.6 | 73.1 | 97.7 |
| 6-7.5 | 151 | 36 | 2 | 2 | 23.8 | 73.5 | 97.3 |
| 10 | 21 | 5 | 0 | 1 | 23.8 | 71.5 | 95.3 |
| 15 | 3 | 0 | 0 | 0 | 0.0 | 100.0 | 100.0 |
| Total | 421 | 106 | 5 | 5 | 25.1 | 72.4 | 97.6 |

since other patients in the series received less than the prescribed dose of serum and in some instances received it late in the period of incubation and still had the disease in modified form. Nevertheless, there undoubtedly is a quantitative element in serum therapy dependent on the susceptibility of the subject, the intimacy of the contact, the size of the infecting dose, the length of exposure, the potency of the serum and possibly other factors which frequently are overlooked.

Table 2 shows the number of inoculated exposed persons and the resulting attacks of modified and unmodified measles in relation to the doses of serum employed. It is to be observed that the percentage of cases of modified measles increased with the decrease in the dose of the serum. The largest percentage of cases of modified measles and the percentage of modification and complete protection occurred in all age groups singly and as a whole when the minimal dose, from 2.5 to 4 cc. of serum, was used. However, the total number of cases in which from 2.5 to 4 cc. was given was too small to warrant the conclusion that these doses are ideal for universal application.

Variations in the size of the dose in the age group under 3 years altered comparatively little the percentage of children who contracted modified measles and of exposed children who escaped infection. In this group, apparently the smaller quantities of serum were almost as effective as the larger. On the other hand, the percentage of modification and of complete protection which occurred in the next two age groups, from 3 to 5 and from 5 to 9 years, appeared to be more definitely correlated with the size of the dose employed (table 3). Each of the last two groups exceeded any other age group by 10 per cent in exposed persons who contracted modified measles (table 1). Undoubtedly the high susceptibility in these age groups, both to infection and to variations in the dose of the serum, were factors contributing to this result.

Table 4 shows the number of inoculated exposed persons who received the doses of serum recommended at the beginning of the analysis and the resulting percentage of cases of modified and unmodified

TABLE 3.—*Results of Prophylaxis According to Age Group and Dose of Serum*

| Dose, Cc. | Percentage Receiving Complete Protection | | | Percentage Having Modified Measles | | |
|---|---|---|---|---|---|---|
| | Under 3 Years | 3-5 Years | 5-10 Years | Under 3 Years | 3-5 Years | 5-10 Years |
| 2.5-4 | 71.5 | 42.9 | 50.0 | 28.5 | 57.1 | 50.0 |
| 5 | 78.3 | 64.9 | 61.9 | 20.1 | 35.1 | 30.9 |
| 6-7.5 | 73.7 | 73.1 | 68.5 | 26.3 | 24.3 | 26.8 |
| Greatest difference in variations | 6.8 | 30.2 | 18.5 | 8.4 | 32.8 | 23.2 |

measles with relation to the length of time which elapsed between exposure and the administration of serum. The same items are shown in table 5 for exposed persons who received less than the recommended doses of serum.

Complete protection from the disease was attained by 75.2 per cent of the group receiving the recommended doses, as compared to 66.2 per cent of the group receiving less than the recommended doses.

Of the exposed persons who received the recommended doses, 22.7 per cent contracted modified measles, as compared to 30.6 per cent of those who received less than the recommended doses. In the first group, 24.8 per cent contracted the disease (modified or unmodified measles), as compared to 33.8 per cent in the second group. From this it may be noted that, while a higher percentage of cases of modified measles occurred in persons who received less than the recommended doses of serum, a slightly higher percentage of cases of unmodified measles occurred also.

Until further observations are carried out, a statement cannot be made as to what is the optimum dose to use in each age group in order to obtain the highest percentage of modified measles and the lowest per-

centage of unmodified attacks. The answer to this question may have to await the standardization of pooled serums. Nor are the results of this study uniform enough to enable us to state what is the ideal time in the period of incubation at which to administer serum to obtain the

TABLE 4.—*Results of Prophylaxis with the Recommended Doses of Serum with Relation to the Day of Exposure and of the Administration of Serum*

| Day of Exposure | Exposed Persons | Modified Measles | Unmodified Measles | Modified Measles, Percentage | Modified and Unmodified Measles, Percentage |
|---|---|---|---|---|---|
| Less than 1 day | 6 | 3 | 0 | 50.0 | .... |
| 1 | 29 | 6 | 0 | 20.6 | .... |
| 2 | 30 | 6 | 0 | 20.0 | .... |
| 3 | 32 | 7 | 1 | 21.8 | 25.0 |
| 4 | 40 | 2 | 0 | 5.0 | .... |
| 5 | 53 | 14 | 2 | 26.0 | 30.1 |
| 6 | 40 | 7 | 1 | 17.5 | 20.0 |
| 7 | 40 | 16 | 0 | 40.0 | .... |
| 8 | 9 | 2 | 0 | 22.2 | .... |
| 9 | 3 | 1 | 0 | 33.3 | .... |
| 10 | 2 | 1 | 0 | 50.0 | .... |
| 11 | 1 | 0 | 0 | .... | .... |
| 13 | 1 | 1 | .. | 100.0 | .... |
| 14 | 0 | 0 | .. | .... | .... |
| Unknown | 9 | 2 | 2 | 22.2 | 44.4 |
| Total | 294 | 67 | 6 | 22.7 | 24.8 |

Complete protection, 75.2%; modified measles, 22.7%; unmodified measles, 2.04%.

TABLE 5.—*Results of Prophylaxis with Less than the Recommended Doses of Serum with Relation to the Day of Exposure and of the Administration of Serum*

| Day of Exposure | Exposed Persons | Modified Measles | Unmodified Measles | Modified Measles, Percentage | Modified and Unmodified Measles, Percentage |
|---|---|---|---|---|---|
| Less than 1 day | 1 | 1 | 0 | 100.0 | .... |
| 1 | 8 | 1 | 0 | 12.5 | .... |
| 2 | 9 | 0 | 0 | .... | .... |
| 3 | 16 | 2 | 0 | 12.5 | .... |
| 4 | 21 | 7 | 0 | 33.3 | .... |
| 5 | 21 | 8 | 1 | 38.0 | 42.8 |
| 6 | 24 | 5 | 1 | 20.8 | 25.0 |
| 7 | 19 | 10 | 2 | 52.6 | 63.1 |
| 8 | 2 | 2 | 0 | 100.0 | .... |
| 9 | 0 | 0 | .. | .... | .... |
| 10 | 0 | 0 | .. | .... | .... |
| 11 | 0 | 0 | .. | .... | .... |
| 13 | 0 | 0 | .. | .... | .... |
| 14 | 1 | 1 | 0 | 100.0 | .... |
| Unknown | 2 | 1 | 0 | 50.0 | .... |
| Total | 124 | 38 | 4 | 30.6 | 33.8 |

Complete protection, 66.2%; modified measles, 30.6%; unmodified measles, 3.2%

maximum percentage of modified attacks. The number of patients receiving injections on several different days was too small to permit generalizations. If one disregards in tables 4 and 5 the groups con-

sisting of less than 10 persons, one finds on the whole that the highest percentage of cases may be expected to occur in persons given injections after the fourth or fifth day of the period of incubation. Modified measles occurred in the 2 patients who received serum on the thirteenth and fourteenth days of incubation.

### THERAPY

Seven patients were given serum after the onset of the disease. The results are shown in table 6. The course was modified in 4 cases and unaffected in 3. In the group in which it was modified, the serum was given during the period of invasion, when Koplik's spots or fever was present but before the rash appeared. Study of the group in which it was unmodified reveals that in 1 case the child had bronchopneumonia prior to the development of measles and, in addition, did not receive convalescent serum until after the rash had been present for two days.

TABLE 6.—*Results in 7 Cases of Serum Therapy*

| No. | Age, Years | Stage of Disease in Which Serum Was Given | Amount of Serum, Cc. | Modified Measles | Unmodified Measles | Complications |
|---|---|---|---|---|---|---|
| 378 | 3 | Disease present 1 day | 5 | Mild | .. | None |
| 110 | 4 | Koplik's spots present | 7.5 | Mild | .. | None |
| 30 | 5 | Koplik's spots present | 7.5 | Modified | .. | None |
| 360 | 6 | Koplik's spots present | 15 | Mild | .. | None |
| 119 | 6 | Rash present 2 days | 20 iv. | ..... | + | Bronchopneumonia previously |
| 120 | 3½ | Late in disease; patient in coma | 10 | ..... | + | Died on third day |
| 89 | 12 | Fever and coryza 1 day | 5 | ..... | + | None |

This is too late in the course of the disease to hope for much benefit. The second child was not given serum until the disease had reached an advanced stage, at which time he was in a state of coma. Death intervened three days later. The third child was not given a sufficient amount of serum for therapeutic results. Although 12 years old, she received only 5 cc. of serum, which is less than the prophylactic dose recommended for that age. Even prophylactic doses vary according to the length of time between exposure and administration. With longer intervals, larger amounts of serum are required to give complete protection and still larger doses are probably necessary to afford therapeutic benefit.

Although the group of patients for whom data are given in this table is too small to permit definite conclusions, the results indicate that convalescent serum may be of therapeutic value.

### COMMENT

It is to be hoped that convalescent serum will be used in the future with the idea of inducing modified measles to establish permanent immunity rather than of attempting to bestow complete protection, which

may afford only temporary immunity. This is especially desirable with children above 5 years of age who have no debilitating disease or condition which would make it unwise for them to have measles.

Many of the older children in the series reported on were given serum for complete protection at the request of the parents, because measles would have interfered with vacation plans. The adults who received passive immunization also desired complete protection. These are justifiable exceptions to the policy advocated and will always be found in similar groups of cases.

In order that the real therapeutic value of serum may be established, we would like to see more patients receive it after the onset of the disease, in which case injections should be made early in the prodromal period, before the appearance of the rash.

## CONCLUSIONS

1. Our findings corroborate the good results obtained by others with the use of convalescent serum.

2. At least 97.7 per cent of the subjects benefited from the injection of serum: 72.5 per cent received complete protection, and 25.2 per cent had modified measles.

3. Modified measles may be attained by regulation of the dose of serum, by the late injection of serum, or by the combination of both measures. Further observations are necessary for the achievement of greater success in the regulation of these two factors.

4. Inoculation with convalescent serum is the best preventive measure known against measles because of its high protective value, the resulting low incidence of complications and the absence of serum reactions. Furthermore, it may possess therapeutic value.

# HUMAN PASSIVE TRANSFER ANTIBODY

## I. TITRATION BY NEUTRALIZATION

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The presence of the passive transfer antibody of human hypersensitivity may be readily detected by the technic of Prausnitz and Küstner.[1] An appraisal of its significance in the course of allergic diseases depends, however, on the introduction of methods for quantitative determination.

Levine and Coca [2] introduced two methods, which involved dilution of serum and of antigen, respectively. The first depended on the injection of progressive dilutions of serum into the skin of a normal recipient and subsequent injection of a fixed quantity of antigen into the sensitized areas. The second depended on the reaction produced by injecting progressive dilutions of antigen into areas of normal skin previously sensitized by injection of constant amounts of serum. The results of titrations with these technics were sometimes difficult to interpret because of indefinite end-points obtained on local injection of antigen.

Since it was known that the passive transfer antibody might be neutralized by its specific antigen,[3] Woringer [4] suggested a method of titration dependent on this principle and applied it to the study of infantile eczema associated with sensitivity to egg white. The neutralization of the antibody instead of its dilution should evoke more definite end-points.

The purpose of this investigation was to develop and more clearly define a method of neutralization which might be applied in studies of clinical hypersensitivity associated with a variety of antigens.

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1. Prausnitz, C., and Küstner, H.: Studien über die Ueberempfindlichkeit, Centralbl. f. Bakt. (Abt. 1) **86**:160, 1921.

2. Levine, P., and Coca, A. F.: Studies in Hypersensitiveness: XXI. A Quantitative Study of the Atopic Reagin in Hay Fever; the Relation of Skin Sensitivity to the Reagin Content of Serum, J. Immunol. **11**:435, 1926.

3. Coca, A. F., and Grove, E. F.: Studies in Hypersensitiveness: XIII. A Study of the Atopic Reagins, J. Immunol. **10**:445, 1925.

4. Woringer, P.: Méthode de dosage de l'anticorps ovalbuminique dans le sang des sujets allergiques au blanc d'oeuf, Ann. Inst. Pasteur **50**:270, 1933.

TECHNIC

The technic developed for titration of the passive transfer antibody is briefly outlined in the following paragraphs. Experiments controlling several factors involved are discussed later.

1. *Preparation of Serum.*—Blood is obtained from patients with allergic disorders; the serum is separated and stored in sterile rubber-capped vials.

2. *Preparation of Antigen Dilutions.*—Concentrated antigen solutions of known nitrogen concentration, prepared within six months, are freshly diluted when mixtures are to be made. The stock solution is diluted so that 1 cc. contains 0.15 mg. of total nitrogen. Progressive dilutions of the stock solution are prepared as follows: 1:2, 1:5, 1:10, 1:20, 1:50, 1:100 and 1:1000. The diluent is physiologic solution of sodium chloride containing merthiolate in a concentration of 1:2000.

3. *Preparation of Antigen-Antibody Mixtures.*—Four-tenths cubic centimeter of undiluted serum is placed in each of seven vials; 0.1 cc. of one of the antigen dilutions previously mentioned is added to each vial. The final dilutions of stock antigen solution in the mixtures are as follows:

| | Mg. of Antigen Nitrogen per Cubic Centimeter |
|---|---|
| 1:10 | 0.015 |
| 1:25 | 0.006 |
| 1:50 | 0.003 |
| 1:100 | 0.0015 |
| 1:250 | 0.0006 |
| 1:500 | 0.0003 |
| 1:5,000 | 0.00003 |

The term antigen nitrogen designates the total nitrogen in the serum-antigen mixtures which is derived from the antigen solution.

The final dilution of merthiolate in the mixtures is 1:10,000.

4. *Injection of Mixtures.*—One-tenth cubic centimeter of each mixture is injected intracutaneously at intervals of approximately 5 cm. into the arms of three recipients. Persons chosen as recipients are in good health and have no history of allergic disorders. When the antigen concerned is a food, it is eliminated from the recipients' diets until the subsequent injection.

5. *Injection of Antigen.*—Secondary injections of antigen are administered from one to three days after the injection of the antigen-antibody mixtures. As a preliminary test, to exclude the possibility of natural sensitivity, recipients are tested endermally with 0.02 cc. of a strong concentration of the antigen (containing 0.3 mg. of nitrogen per cubic centimeter). If no significant local reaction appears, the same solution is injected intramuscularly into the external aspect of the thigh. Older

children and adults receive injections of 3 cc., and children under 10, injections of 1.5 cc. The sites previously sensitized with serum-antigen mixtures are then observed for wheals, which may appear from twenty minutes to two hours later. The dimensions of the reactions are recorded. The titer of the serum is based on the antigen concentration of the mixture at the site above the first wheal. The method of recording titrations is discussed in detail later.

## EXPERIMENTAL CONTROLS AND DEFINITIONS

*Standardization of the Antigen Solutions.*[5]—Since different materials yield different concentrations of antigenic substance on extraction, one of the methods of antigen standardization must be utilized. Although available evidence does not clearly establish its superiority, the method involving the total nitrogen content advocated by Coca [6] and others was adopted. The technic for antibody titration described, however, is applicable to other methods of antigen standardization.

*Method of Reading Titrations.*—After the intramuscular injection of antigen into the locally sensitized recipient, wheals appear at the sites of previous injections in which the solution contained insufficient antigen to neutralize the antibody completely. In these areas the antibody remains free to sensitize the cells, and a reaction occurs when the antigen, which is absorbed into the circulation after intramuscular injection, comes in contact with the sensitized tissues. Where complete neutralization of the antibody occurs, no reaction is observed. The dilution of the antigen at which there is complete neutralization of the antibody without an excess of antigen lies between the last reacting and the first nonreacting site. For the sake of uniformity, the smallest concentration of antigen which completely neutralizes the serum is considered the end-point. The titer of the serum is therefore based on the antigen concentration of the mixture at the first nonreacting site.

The protocol of a typical titration is recorded in table 1. The reactions which appeared in one of the recipients after the intramuscular injection of antigen are illustrated in the figure.

As a means of recording the titer, a unit system is suggested. One unit of the passive transfer antibody is defined as the amount neutralized by the quantity of antigen that contains 0.00001 mg. of total nitrogen.[7] The titer of a serum is recorded as the number of units of antibody per cubic centimeter of antigen-antibody mixture. When one is dealing with

5. The Arlington Chemical Company, Yonkers, N. Y., made many of the antigens used in this study.

6. Coca, A. F.: A New Definition of the Noon Pollen Unit, J. Allergy **5**:345, 1934.

7. This unit is, of course, constant only for the antibody related to a certain antigen or to a group of antigens. For example, it cannot be assumed that 1 unit of pollen antibody is equivalent to 1 unit of egg white antibody.

pollens, 1 unit of antibody is neutralized by 1 Noon pollen unit, as recently defined by Coca.[6] Final antigen dilutions containing from 0.00003 to 0.015 mg. of nitrogen per cubic centimeter, covering a range of titration from 3 to 1,500 units, are adequate for the majority of serums. Mixtures containing higher concentrations of antigen may be injected when indicated.

As previously noted, all titrations are done in triplicate. This eliminates the possibility of false results from the use of a person with nonreactive skin as recipient. Only seven of a group of four hundred normal persons tested failed to accept any degree of local sensitization.

Practically, dilutions cannot be graduated so closely that the exact point of neutralization is included in one of the mixtures. The skin of one easily sensitized recipient may therefore be slightly sensitized by a

TABLE 1.—*Protocol of a Typical Titration of Passive Transfer Antibody*

| | Recipient 1 | | Recipient 2 | | Recipient 3 | |
|---|---|---|---|---|---|---|
| Mixtures injected..... | Dec. 9, 1935 | | Dec. 9, 1935 | | Dec. 9, 1935 | |
| Endermal test..... | Wheal.... 4×3 mm.<br>Erythema 0 | | Wheal.... 5×5 mm.<br>Erythema 8×8 mm. | | Wheal.... 5×5 mm.<br>Erythema 7×7 mm. | |
| Intramuscular injection... | 1.5 cc. of ragweed (nitrogen = 0.3 mg. per cc.) | | 1.5 cc. of ragweed (nitrogen = 0.3 mg. per cc.) | | 1.5 cc. of ragweed (nitrogen = 0.3 mg. per cc.) | |
| Date..... | Dec. 10, 1935 | | Dec. 10, 1935 | | Dec. 10, 1935 | |
| Antigen nitrogen per cubic centimeter of mixture | Wheal, Mm. | Erythema, Mm. | Wheal, Mm. | Erythema, Mm. | Wheal, Mm. | Erythema, Mm. |
| 0.01500 mg. | 0 | 0 | 0 | 0 | 0 | 0 |
| 0.00600 mg. | 0 | 0 | 0 | 0 | 0 | 0 |
| 0.00300 mg. | 0 | 0 | 0 | 0 | 0 | 0 |
| 0.00150 mg. | 0 | 0 | 0 | 0 | 0 | 0 |
| 0.00060 mg.* | 0 | 0 | 0 | 0 | 0 | 0 |
| 0.00030 mg. | 25×15 | 40×40 | 8×6 | 35×20 | 30×25 | 50×40 |
| 0.00003 mg. | 40×30 | 60×50 | 32×20 | 50×45 | 36×30 | 50×50 |

* Titer of serum = 60 units.

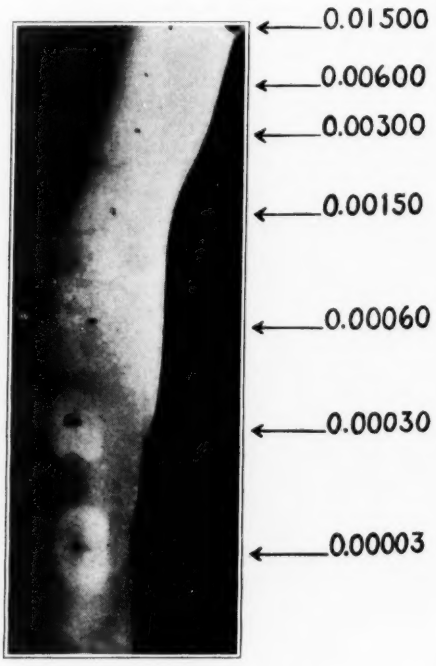
mixture containing a small excess of antibody, which fails to sensitize the other two. When the end-points are not identical, and they seldom differ by more than one gradation, the titer is based on the majority of the reactions.

*Standardization of the Intramuscular Injection.*—Several recipients received an intracutaneous injection of 0.1 cc. of each of the usual series of antigen-antibody mixtures, and twenty-four hours later they received intramuscular injections of various amounts of the specific antigens. Three cubic centimeters of antigen solution containing 0.3 mg. of nitrogen per cubic centimeter was found adequate to produce reactions at sensitized sites in adults and 1.5 cc. to produce reactions in children under 10 years. The subsequent injection of a larger amount failed to produce a reaction in a previously nonreactive site.

Identical results were observed when persons of various weights were used as recipients for the same titration. If the result depended only on the dilution of the antigen in the circulation, the sensitized tissues

of the larger recipients would be stimulated by much less antigen than the same tissues of the smaller recipients. Over a period of several minutes, however, a much larger amount of antigen than is calculated on the basis of dilution in the circulation may come in contact with these tissues, and the resultant reactions may depend on stimulation of the sensitized tissues by amounts far in excess of those estimated on that basis.

One hundred and seventeen recipients were tested intracutaneously at frequent intervals for three months after the intramuscular injec-




Reactions which appeared in recipient 3 after the intramuscular injection of antigen (table 1). The figures indicate milligrams of antigen nitrogen per cubic centimeter in the serum-antigen mixtures injected on the previous day.

tion of a variety of antigens. Six showed small, transient increases in the intensity of the cutaneous reactions. Data on these subjects will be presented in detail in a subsequent paper.

One generalized reaction was encountered in a group of approximately four hundred recipients who received intramuscular injections. This reaction was observed after the injection of peanut extract and was characterized by urticaria and asthma, both of which were promptly relieved by the administration of epinephrine. In this recipient a positive endermal reaction to peanut subsequently developed.

*Stability of the Antigen-Antibody Mixture.*—In order that we might determine how long a mixture of serum and antigen may remain in storage without alteration in the titer, six titrations were repeated after an interval of from two to six months. In each instance, the result of the second titration was identical with that of the original titration. One is led to conclude from these data that titrations may be accurately completed at least several weeks after the mixture is made.

*Specificity of Neutralization.*—The experiment of which the report follows demonstrated the absence of nonspecific neutralization of the passive transfer antibody in titration mixtures. Serums containing antibodies for both egg and peanut were titrated for each one separately. Ten recipients of the egg-serum mixtures subsequently received intramuscular injections of peanut extract, and ten recipients of peanut-serum mixtures received subsequent injections of egg white. After injection of the second antigen, from seven to forty-five days later, reactions occurred in all the areas of local injection, although reactions had previously occurred only at the sites into which a mixture containing an excess of free antibody had been injected. This experiment is in agreement with the accepted theory that the passive transfer antibody is specific for its corresponding antigen.

The second antigen was injected from seven to ninety days after the injection of the serum-antigen mixtures. Reactions invariably occurred up to forty-five days after sensitization but never after sixty days. One is led to conclude from this observation that normal skin may remain sensitized for approximately forty-five days.

*Comparison of the Neutralization Technic with the Serum Dilution Method.*—In order that we might compare the neutralization technic previously described with the serum dilution method in current use, twelve serums were titrated by the two methods. In eight serum dilution titrations, 0.1 cc. of progressive serum dilutions was injected endermally into the back of each of two or more recipients. Twenty-four hours later, an injection was given at each site of 0.025 cc. of antigen containing 0.004 mg. of total nitrogen per cubic centimeter, and the reactions were measured after fifteen minutes. Similar amounts of antigen were also injected into the upper and the lower portion of the back as controls.

In four serum dilution titrations, an interval of three days was allowed to elapse between the injection of the serum and the injection of a stronger concentration of antigen (0.05 mg. of total nitrogen per cubic centimeter).

The results of these observations are recorded in table 2. In the serum dilution titrations, it was difficult to obtain definite end-points after local injection, and considerable variation between the reactions of different recipients was noted. In general, however, the average

titers obtained by the serum dilution method roughly paralleled those obtained by the neutralization method, and serums of high neutralizing power tolerated greater dilution before they failed to produce demonstrable sensitization. Serums which showed the same titer by neutralization did not, however, show identical titers by the other method. Culbertson [8] observed similar variations in the titers of precipitins obtained by neutralization and those obtained by serum dilution methods.

TABLE 2.—*Titration of the Same Serums by Neutralization and Serum Dilution Methods*

| Serum | Antigen | Titer by Neutralization Method, Units | Average Titer by Serum Dilution Method, Greatest Dilution of Serum Giving a Positive Reaction | Previous Treatment |
|---|---|---|---|---|
| M. S..... | Ragweed | 3 | Less than 1-10 | None |
| A. J..... | Ragweed | 150 | 1-850 | None |
| W. M..... | Ragweed | 600 | 1-325 | Ragweed injections for 1 yr.; last injection 4 mo. previously |
| P. M..... | Ragweed | 600 | 1-600 | Ragweed injections for 6 mo.; last injection 3 wk. previously |
| F. M.*..... | Ragweed | 3 | 1-100 | None |
| E. C.*..... | Ragweed | 60 | 1-200 | Ragweed injections for 5 mo.; last injection 2 wk. previously |
| W. Z.*..... | Ragweed | 150 | 1-300 | Ragweed injections for 11 mo.; last injection 3 mo. previously |
| W. K.*..... | Ragweed | 1,500 | 1-500 | Ragweed injections for 5 mo.; last injection 1 wk. previously |
| W. G. 10/22..... | Peanut | 3 | 1-7 | Peanut orally 7 days previously |
| W. G. 11/19..... | Peanut | 1,500 | 1-30 | Peanut orally 35 days previously |
| J. S. 12/19..... | Peanut | 1,500 | 1-700 | Peanut orally 73, 44 and 9 days previously |
| J. S. 11/14..... | Peanut | 3,000 | 1-1,750 | Peanut orally 38 and 9 days previously |

* In these cases the interval between injection of the serum dilutions and of the antigen was three days, and the antigen solution contained 0.05 mg. of total nitrogen per cubic centimeter. In all other cases the interval was one day, and the antigen solution contained 0.004 mg. of total nitrogen per cubic centimeter.

Because of the recent observations of Cooke and his co-workers [9] regarding the presence of a specific inhibiting antibody in treated hay fever patients, the previous treatment of the patients from whom the serums were obtained is recorded.

8. Culbertson, J. T.: A Quantitative Study of the Precipitin Reaction with Special Reference to Crystalline Egg Albumin and Its Antibody, J. Immunol. **23**:439, 1932.

9. Cooke, R. A.; Barnard, J. H.; Hebald, S., and Stull, A.: Serological Evidence of Immunity with Coexisting Sensitization in a Type of Human Allergy (Hay Fever), J. Exper. Med. **62**:733, 1935.

## APPLICATION

A variety of serums containing the passive transfer antibody were titrated by the technic described. The method was found applicable to the study of serum obtained from patients suffering from hay fever, asthma, urticaria, angioneurotic edema and eczema. Equally good results were obtained in titrating with a variety of antigens, including foods, inhalants and pollens. Results of a random selection from approximately one hundred and fifty titrations are given in table 3.

In investigations in progress the technic presented has been found useful in the study of fluctuations of the passive transfer antibody content of human serums in terms of antigen equivalence. Furthermore, on this method may be based studies of the quantitative aspects of antigen-antibody combinations.

TABLE 3.—*Titers of Miscellaneous Serums*

| Serum | Antigen | Titer, Units | Diagnosis |
|---|---|---|---|
| W. G. | Peanut | 60 | Asthma and urticaria |
| J. S. | Peanut | 3,000 | Asthma and eczema |
| J. S. | Egg | 150 | Asthma and eczema |
| J. P. | Egg | 150 | Eczema |
| P. S. | Egg | 3* | Eczema |
| S. F. | Codfish | 1,500 | Urticaria |
| F. B. | Horse dander | 300 | Asthma |
| R. P. | Silk | 150 | Asthma and eczema |
| P. M. | Ragweed | 1,500 | Hay fever |
| R. C. | Ragweed | 3* | Hay fever |
| R. Mc. | Orchard grass | 30 | Hay fever |
| A. C. | Timothy | 3* | Hay fever |

* These serums sensitized normal skin when unmixed yet were neutralized when the serum-antigen mixtures contained as little as 0.00003 mg. of total antigen nitrogen per cubic centimeter.

## SUMMARY

A method is described for the titration of the passive transfer antibody. This method depends on the determination of the amount of antigen necessary to neutralize the available antibody in a given amount of serum. The procedure involves the mixture of various dilutions of antigen with constant amounts of serum in vitro, the intracutaneous injection of the resultant mixtures and subsequent intramuscular injection of the antigen. After intramuscular injection, reactions appear at cutaneous areas where incompletely neutralized serum was injected. The titration level is based on the smallest amount of antigen which inhibits sensitization.

Experiments concerning several factors involved in the technic, such as the standardization of intramuscular injections, the stability of antigen-antibody mixtures and the specificity of neutralization, are described.

The method has demonstrated variations in the titer of the passive transfer antibody in serums of persons hypersensitive to a variety of antigens.

# STUDIES WITH BCG

## IV. THE FOCAL AND THE GENERAL TISSUE RESPONSE AND THE HUMORAL RESPONSE; THE INTRADERMAL ROUTE

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According to Besredka,[1] the organs have receptive cells for certain bacteria, and irrespective of the route of entry of these organisms they become localized in the receptive cells (reticulo-endothelial system) of the specific organs. Coulaud,[2] after injection of virulent and avirulent tubercle bacilli subcutaneously, was able to demonstrate tubercles in the lung, as was Makada.[3] He concluded that the primary tuberculous complex in the lungs is not necessarily a result of bacterial inhalation but may be due to entry of bacteria through the skin, mucous membranes or intestine (a view held by Calmette and the entire French school).

With the widespread employment of BCG for vacination against tuberculosis, it was soon discovered that when the oral method of administration was used only a small percentage of the persons vaccinated reacted to old tuberculin (from 4 to 10 per cent—Calmette and his co-workers,[4] Weill-Hallé [5] and others). Because it was assumed that a positive reaction to the tuberculin test indicated the presence of viable organisms and tubercles in the host and thus a means of detecting the efficacy of the vaccine, parenteral administration of BCG was adopted in numerous clinics (Wallgren,[6] Kereszturi, Park and Schick,[7]

From the Tice Laboratories, a detail of the Municipal Tuberculosis Sanitarium (Dr. Frederick Tice, president), the University of Illinois Department of Bacteriology and Public Health (Dr. Lloyd Arnold, director) and the Research Division of the Department of Health of the State of Illinois (Dr. Lloyd Arnold, director).

1. Besredka, A.: Local Immunization, Baltimore, Williams & Wilkins Company, 1927.

2. Coulaud, R.: Rev. de la tuberc. **1**:819, 1933.

3. Makada, Y.: Beitr. z. Klin. d. Tuberk. **83**:377, 1933.

4. Calmette, A.; Guérin, C.; Boquet, A., and Nègre, L.: La vaccination preventive contre la tuberculose par le "BCG," Paris, Masson & Cie, 1927.

5. Weill-Hallé, B.: Rev. de la tuberc. **3**:164, 1925; personal interview with the author.

6. Wallgren, A.: Value of Calmette Vaccination in Prevention of Tuberculosis in Childhood, J. A. M. A. **103**:1341 (Oct. 27) 1934.

7. Kereszturi, C.; Park, W. H., and Schick, B.: Parenteral BCG Vaccination, Am. J. Dis. Child. **43**:273 (Feb.) 1932.

Heimbeck,[8] Boudouin,[9] Weill-Hallé,[5] Overton[10] and others. With this method of administration (subcutaneous and intracutaneous) the percentage of reactors to tuberculin was high (from 80 to 100 per cent).

Experimentally, studies of the reaction in remote parts of the body caused by BCG injected intradermally have concentrated chiefly on the formation of specific tuberculous nodules (Coulaud,[2] Makada,[3] Clawson[11] and Birkhaug[12]). The problem of this study was to determine the generalized tissue and humoral response following the intradermal inoculation of BCG irrespective of the presence or absence of tubercles. Simultaneously, the local lesion was studied.

In a previous study it was noted that after the oral administration of BCG a definite activation of the reticulo-endothelial system took place, especially in the lungs, liver, spleen and kidneys, despite the absence of sensitivity to tuberculin (Rosenthal[13]). Similarly, with the intravenous method of administration a generalized activation of the reticulo-endothelial system occurred in regions remote from the tubercle bacilli, as was seen histologically (Rosenthal[14]).

## METHOD

Guinea-pigs (weighing from about 300 to 350 Gm.) received intracutaneous injections of 10 mg. of BCG suspended in 0.2 cc. of physiologic solution of sodium chloride. The animals were killed at intervals of one, two, four, five, seventeen, twenty-four and forty-eight hours; three, five, eight, ten, fourteen and eighteen days; one, two, three and eight months, and one year. The cutaneous lesion and the lungs, liver, spleen, lymph nodes and kidneys were examined histologically; they were fixed in Zenker's solution, blocked in paraffin and stained with hematoxylin and eosin and Ziehl-Neelsen's carbolfuchsin-methylene blue stain. The lungs were injected with Zenker's solution before the chest was opened. Cultures of the sterilely removed organs were made in every case (5 per cent sulfuric acid and Löwenstein's medium were used). In a group of animals cultures of the organs were inoculated in series. That is, cultures of the organs of one group were inoculated intraperitoneally into a second group of animals, and cultures of the organs of the second group were inoculated after varying lengths of time into a third group.

Studies of the blood were made at regular intervals to determine the number and percentage of the various white cells (Wright's method; 200 cells were

8. Heimbeck, J.: Ann. Inst. Pasteur **43**:1229, 1929.

9. Boudouin, J. A.: Personal communication to the author.

10. Overton, J.: South. M. J. **24**:878, 1931.

11. Clawson, B. J.: Relation of Allergy and Lesions in Animals Vaccinated with BCG, Arch. Path. **19**:673 (May) 1935.

12. Birkhaug, K. E.: Am. Rev. Tuberc. **27**:6, 1933.

13. Rosenthal, S. R.: Ann. Inst. Pasteur, to be published.

14. Rosenthal, S. R.: Focal and General Tissue Responses to an Avirulent Bacillus, Arch. Path. **22**:348 (Sept.) 1936.

counted). The rate of sedimentation was determined by a Landau apparatus. Blood for culture was taken from one hour to fifteen days after the inoculation.

The cells of the abdominal fluid removed sterilely with a Pasteur pipet were studied in the following way: Vital staining with neutral red was followed by staining with Wright's method to determine the type of cells present, and the cells were counted in a counting chamber.

A second group of guinea-pigs were treated in exactly the same manner as the first group except that the organisms (10 mg. in 0.2 cc. of physiologic solution of sodium chloride) were injected subcutaneously.

To rule out the influence of manipulation, a third group of animals were given intracutaneous injections of BCG and were killed at regular intervals in the manner described without the performance of any other tests.

Thirty-five animals were thus studied in detail.

## RESULTS

After the intracutaneous injection of BCG as verified by microscopic examination, it was observed that these organisms soon extended by way of the lymphatics to the subcutaneous and the muscular tissues, a fact not known at the beginning of the experiment. For this reason, the results in the three groups studied are combined. Except for minor variations, they were similar.

### SKIN

*Macroscopic Examination of the Local Lesion.*—The injected suspension of bacilli produced a bleb 10 mm. in diameter which was partly absorbed after two hours and completely absorbed after four hours. Not until seventeen hours had elapsed was an area of induration palpable. The induration progressed, and at forty-eight hours a nodule 8 mm. in diameter and elevated about 3 mm. was apparent. A suggestive fluctuating center was palpable. It was distinct at three days and was accompanied by a circumventing zone of hyperemia. At from four to seven days the material in the central area of liquefaction in about half the animals was discharged through the broken skin. By the second week a well defined crater with clean edges remained. Where ulceration did not occur the area of liquefaction receded. During the third and fourth weeks only a small scar remained, and by the sixth or eighth week the site of inoculation was not discernible as the hair had regrown and obscured it.

*Microscopic Examination of the Local Lesion.*—Shortly after (two hours) the introduction of the bacterial suspension within the connective tissue fibers of the cutis were still spread apart by the fluid. The subcutaneous and the muscular layer appeared edematous, but the majority of the bacilli confined themselves to the reticulum layer of the dermis. Bordering the wide zone of the edema was a narrow rim of fibrin. Polymorphonuclear leukocytes, though not numerous, dispersed themselves in this area. Phagocytosis of the bacillary elements was minimal. These elements were embedded in a blue-staining (Ziehl-Neelsen's stain) granular mass that seemed to inhibit phagocytosis. Remote from the site of inoculation dilated vessels filled with granulocytes prevailed.

At four hours the site of inoculation became better defined, by a broad zone of neutrophils (fig. 1*A*). The bacilli seemed to have increased in number and to have arranged themselves in clumps, and the blue-staining granules were scarce. The microphages showed active phagocytosis of the bacilli and the granules. The

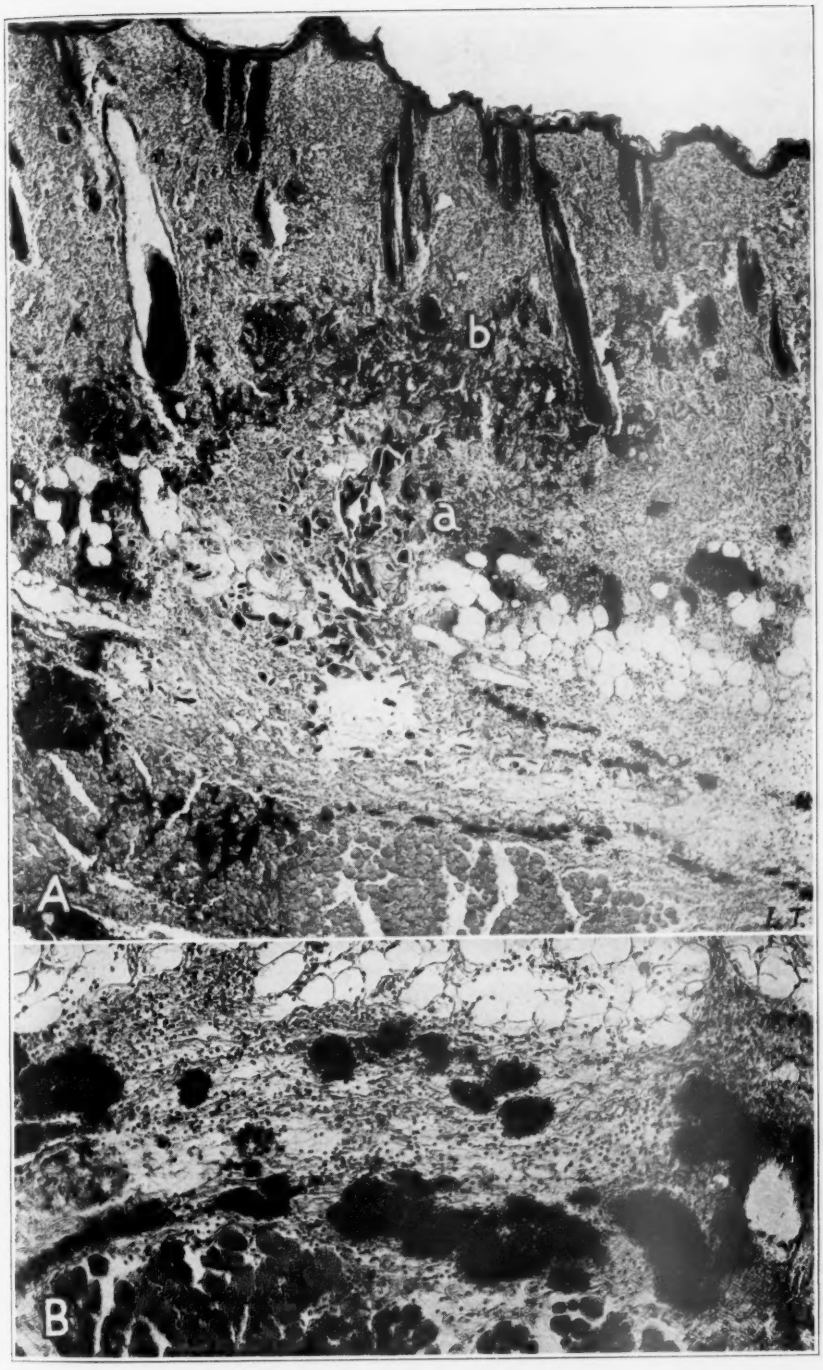


Fig. 1.—*A*, the skin four hours after inoculation with bacilli; × 80. The bacilli are clumped in the reticulum layer of the cutis (*a*), and about them is a broad zone of polymorphonuclear infiltration (*b*). *B*, the edge of the skin above the lesion; × 180. Note the lymphatics of the subcutaneous tissue stuffed with granulocytes. (The Ziehl-Neelsen stain revealed numerous phagocytosed bacilli.) These sections and those shown in the subsequent figures were stained with hematoxylin and eosin.

lymphatics in the area surrounding the site of inoculation and extending to the subcutaneous tissue and the muscularis were widely dilated and filled with these phagocytic cells (fig. 1 *B*). In regions from 2 to 4 cm. from the center of pathologic change, perivascular histiocytes showed active proliferation. The fibrocytes of the cutis became swollen and their nuclei vesicular, resembling histiocytes. Similarly, the cells of the endomysium showed signs of activity by their alterations in structure and by the basophilia of their cytoplasm.

By the seventeenth hour after inoculation the number of bacilli had decreased and the amount of phagocytosis was moderate. The lesion had definitely extended into the subcutis but was well localized by the broad zone of granulocytes, in which were now scattered histiocytic elements (5 per cent). The lymphatics were wide but empty. As the process progressed (for twenty-four hours) the number of histiocytes increased to 10 per cent, and by the forty-eighth hour the periphery of the nodule was composed of equal numbers of granulocytes and histiocytes. The center of the nodules was composed of degenerated pus cells and acid-fast and nonacid-fast bacilli and granules. The lesion now embraced the cutis, the subcutis and the muscular layers.

At from three to eight days the pathologic changes present were not dissimilar to those described, except that more pus had accumulated, and the phagocytosis was affected by the histiocytes, the latter having engulfed the pus cells and the bacillary forms. Extensions from the well localized lesion had been executed by granulocytes filled with bacilli. The remote response was similar but further advanced (fig. 2).

By the end of the second week the few remaining bacilli and granules were all phagocytosed by the epithelioid cells, which constituted 75 per cent of the granuloma. The epithelioid cells presented marked pleomorphism, and the formation of giant cells, some of the Langerhans variety, occurred (fig. 3 *A*). Lymphocytes, fibrocytes and even fibrous tissue surrounded the lesions. In the muscularis the muscle fibers had degenerated and had been replaced by fibrocytes and giant cells. Hemorrhages were observed surrounding and to a less extent within the granuloma in animals killed in the face of a positive reaction to the tuberculin test (fig. 3 *B*). Toward the third week the number of giant cells had definitely increased, many being of the Langerhans type. Areas of central degeneration were again noted, but this time they were due to degenerated epithelioid cells. Gradually the nodule became smaller, and the proportion of lymphocytes, fibrocytes and fibrous tissue increased. At this stage histiocytes containing an occasional bacillus were observed remote from the granuloma.

By the end of the first month the granuloma was composed mainly of fibrocytes and fibrous tissue. Langerhans' giant cells and a few epithelioid cells were observed. The muscle fibers undergoing degeneration presented many giant cells (fig. 4). The remote reaction had subsided.

By the fifth week there was no evidence of tuberculosis. All that remained was scarring of the reticular layer of the cutis, the subcutis and the muscularis, and a slight depression of the regenerated epidermis. From the fifth week on the hair regrew, and only slight fibrosis was present in the skin and the muscularis.

*Fate of the Bacilli.*—The organisms used for inoculation were in general acid-fast and granular, though there were some nonacid-fast forms. Two hours after their introduction into the body their acid-fast characteristic was lost to a great extent, and the bacilli were embedded in a circumscribed accumulation of blue-staining granules. There was little or no phagocytosis. At four hours the number of acid-fast bacilli seemed to have increased. The bacilli were arranged in clumps, and the blue-staining granules were definitely reduced in number. Phago-

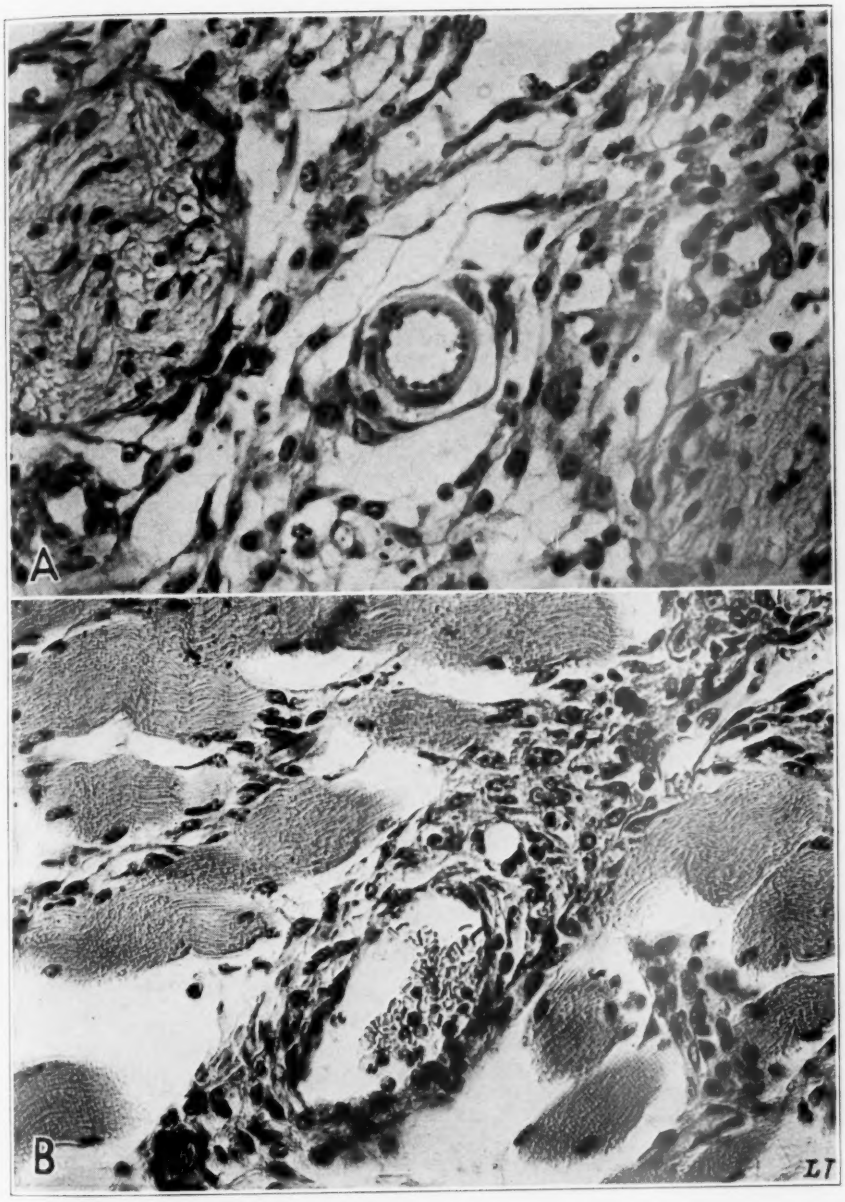


Fig. 2.—*A*, the skin three days after inoculation; × 360. *A* shows perivascular and perineural histiocytic proliferation remote from the site of inoculation. *B* shows muscle fibers with histiocytic proliferation of the endomysium. Note also the perivascular cellularity.

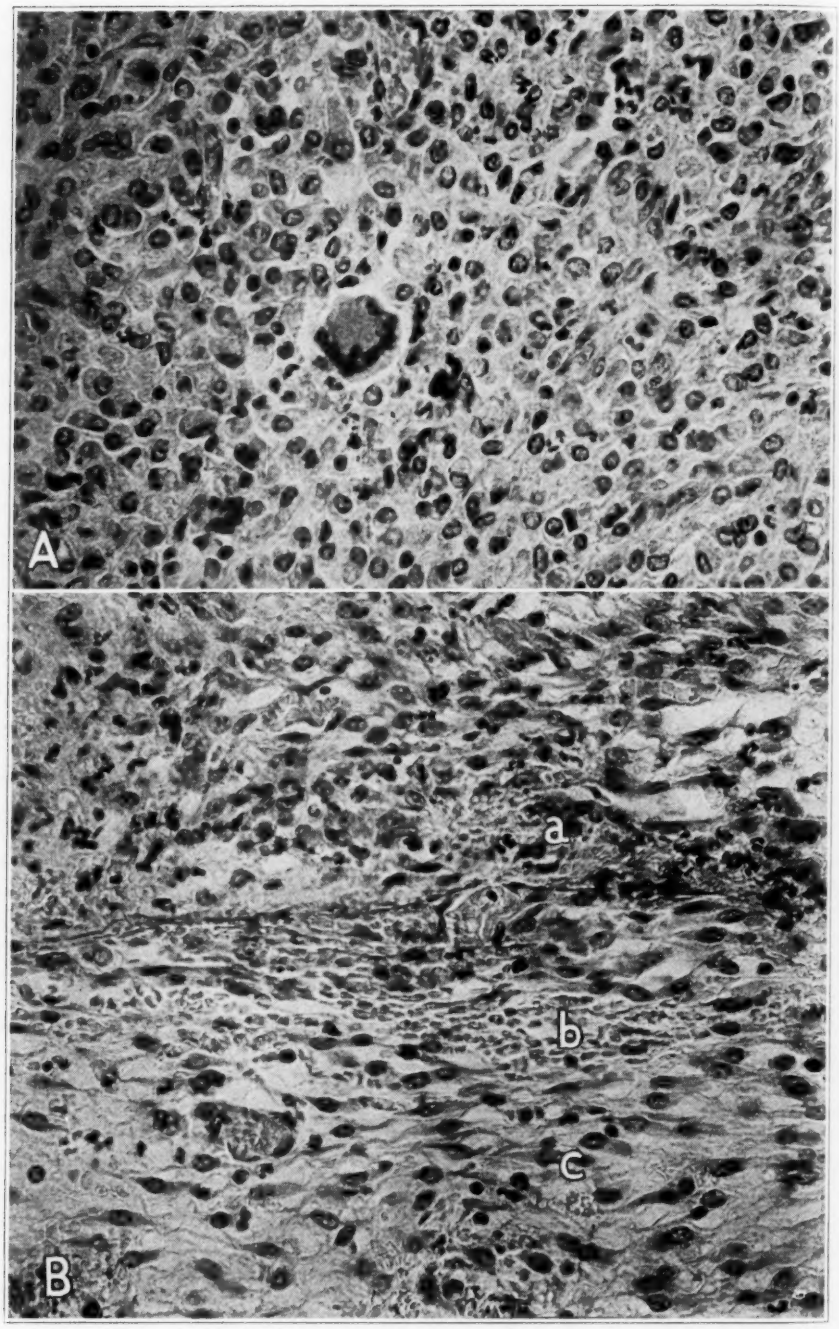


Fig. 3.—*A*, typical tuberculous granuloma of the skin eighteen days after inoculation; × 360. Note the Langerhans giant cells. *B*, the skin fourteen days after inoculation; × 360. Note the edge of the granuloma (*a*) and the extravasation of blood (*b*). The histocytic response of the connective tissue surrounding the granuloma is indicated by *c*. The reaction to the tuberculin test was positive on the day the animal was killed.

cytosis was now active by the polymorphonuclear leukocytes. From this time on the number of bacilli gradually diminished. They became more granular and lost their acid-fast character, and finally, at eighteen days, only blue-staining granules and an occasional bacillus were observed. At twenty-seven days and thereafter neither bacilli nor granules were observed.

Shortly after the inoculation of bacilli phagocytosis was carried out by granulocytes. By the seventeenth hour histiocytes also participated, and by the second week practically all the phagocytosis was carried out by these cells and giant cells. The extension of the process by the microcytes and the macrocytes carrying bacilli followed the same sequence.

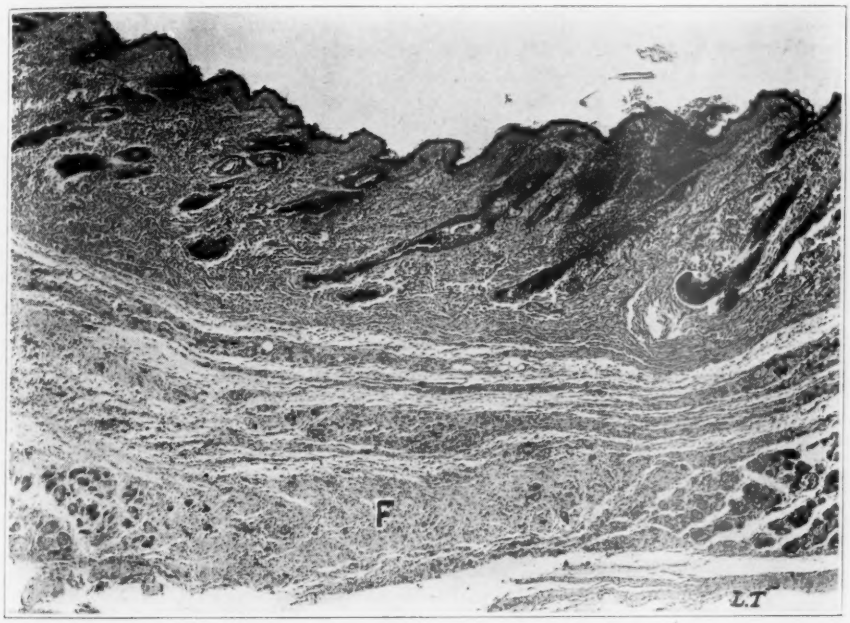


Fig. 4.—Site of inoculation after twenty-seven days; × 44. Note the replacement of the muscle and the subcutaneous tissue by fibrous tissue (*F*). Scattered in the scar tissue are giant Langerhans and muscle cells.

Cultures of a mixture of all the internal organs (not the local lesion), including lymph nodes, were negative except in one instance. In another instance smears of the surface of the medium revealed acid-negative bacilli suggestive of BCG. There was no gross evidence of growth, however. Blood cultures taken from fifteen animals at intervals of from one hour to fifteen days failed to reveal tubercle bacilli.

### INTERNAL ORGANS

*Macroscopic Examination.*—Grossly, the internal organs showed no characteristic alterations. The lymph nodes at the bifurcation of the aorta became swollen and slightly hyperemic two days after the inoculation and remained so for the first week. At eight days the hyperemia had subsided, and the return to normal size was rapid. The posterior tracheal, the mesenteric and the cervical lymph

nodes, as well as the spleen, were slightly enlarged in some instances at the beginning of the experiment, but no significance could be ascribed to these alterations as they were found with equal frequency in the control animals.

*Microscopic Examination of the Lungs.*—Normally, the septal cells were pavement-like and the alveolar walls thin. One hour and twenty minutes after the introduction of BCG slight hyperemia was manifest, and the septal cells in focal areas assumed oval or spherical shapes. At two hours and fifteen minutes the hyperemia subsided, but the swelling of the septal cells continued. The cytoplasm of these cells became slightly basophilic. During the interval from four to seventeen hours after inoculation the process developed to the extent of the formation of small clusters of histiocytic cells at the junction of the alveolar walls. At the end of the first day the septal cells seemed to bulge into the alveolar space (fig. 5). For the next six days there was no change, but at from eight to fourteen days, at about which time allergy set in, the alveolar walls appeared thickened as a result of swelling and proliferation of the septal cells, as well as intracapillary cellularity. Not all the lung reacted in a similar way, some areas showing more reactivity than others. From this time on there was a gradual recession of the process, so that at from four to eight weeks it had subsided.

After the appearance of allergy the injection of old tuberculin was followed by hyperemia and to a less extent by swelling of the septal cells (fig. 6*A*). These changes were marked in the first few weeks of allergy and moderate after from eight to twelve months. In one instance (one year after inoculation) the lung was studded with innumerable lymph nodules with germinal centers, and moderate hyperemia was present, in the face of a 3 plus reaction to tuberculin.

Subpleural areas of atelectasis, in which lymph follicles with germinal centers of various sizes formed the nucleus, were observed in a high percentage of the animals studied. Atelectasis was also observed frequently in control animals. In such areas there appeared to be swelling of the septal cells, interstitial lymphocytic infiltrations and shedding into the alveolar spaces of large monocytic cells, which sometimes closely resembled epithelioid cell tubercles (fig. 6*B*). Such lesions might easily have obscured true tubercles.

*Microscopic Examination of the Liver.*—Rounding of the Kupffer cells and the perivascular histiocytes was observed in the earliest specimen examined (the animal was killed one hour and twenty minutes after inoculation). Progression of this state was slow, and it was not until seventeen hours after inoculation that active phagocytosis of the red cells and the acid-fast granules was appreciable. The granules, however, were large and globular and were similar to those observed in some controls. From the third to the eighth day, at times as late as the fourteenth day, this reaction reached its height (fig. 7). There was pronounced interstitial cellularity, mainly of the histiocytic variety. At times the histiocytes were arranged in clusters. Lymphocytes also appeared. The recession of the process was slow; by the second month it appeared to have subsided, although focal areas of perivascular histiocytes and lymphocytes were still observed.

Of special interest was the state of the liver in the presence of a positive cutaneous reaction to tuberculin. In a fourteen day and in a one year specimen increased activity was observed. The vessels were dilated and filled with blood. In some instances small extravasations of blood were noted.

*Microscopic Examination of the Kidneys.*—The reaction in the kidneys was sluggish, and although there was some endothelial swelling of the glomerular tufts and the issuing vessels as early as one hour and twenty minutes after the injection of BCG, it was not until three days after that a definite reaction was well estab-

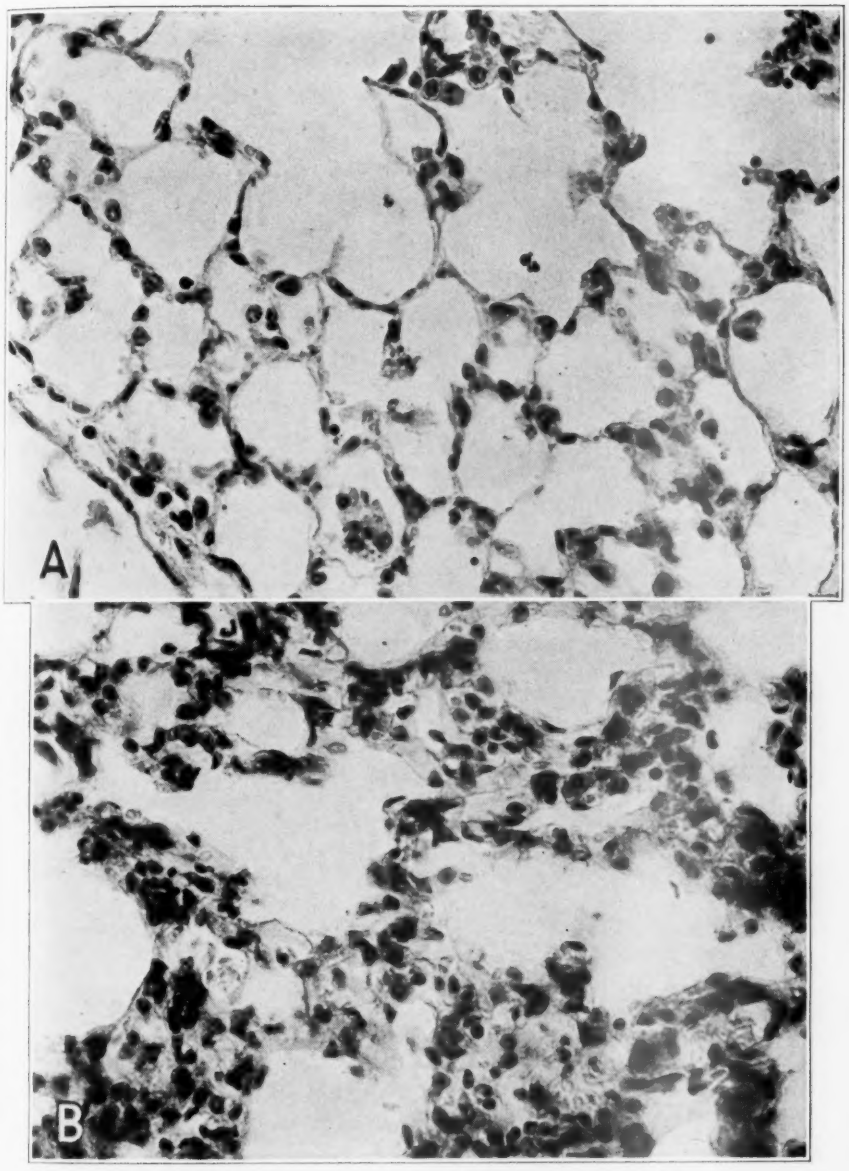


Fig. 5.—*A*, lung twenty-four hours after inoculation; × 360. The alveolar walls are thickened as a result of swelling of the septal cells. *B*, lung forty-eight hours after inoculation; × 360. The thickening of the alveolar walls is a result of intracapillary cellularity as well as of swelling of the septal cells. The process embraced the major portion of one lobe.

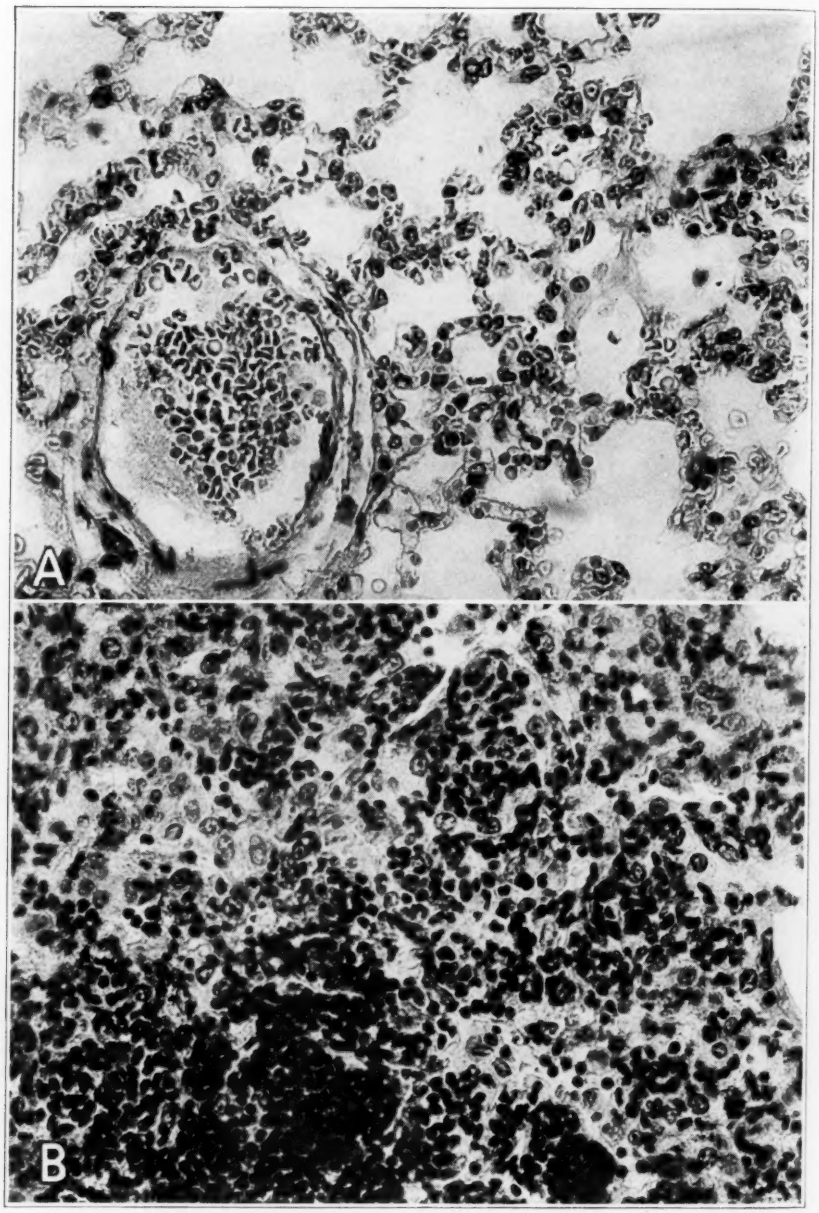


Fig. 6.—*A*, lung fourteen days after inoculation; × 360. The capillaries are diffusely dilated and filled with blood. The reaction to the tuberculin test was positive on the day the animal was killed. *B*, lung two months and thirteen days after inoculation, with a subpleural nodule; × 360. Note the swollen histiocytes surrounded by lymphocytes.

lished (fig. 8 *A*). The glomeruli at this stage were slightly increased in size as a result of hyperemia and swelling of the endothelial cells. The issuing capillaries also presented prominent endothelial cells. The interstitial histiocytes were rounded, increased in number and at times arranged in small groups. This reactivity was found chiefly in the cortex. The peripelvic fat presented more cellularity than is normal, and the histiocytes were well rounded and their cytoplasm basophilic. The process persisted until eight days after inoculation and then gradually subsided, the tissue being practically normal by the eighteenth day.

The introduction of tuberculin affected the kidneys. In two animals killed after one year there were hyperemia and extravasations from the blood, as well as perivascular histiocytic swelling (fig. 8 *B*).

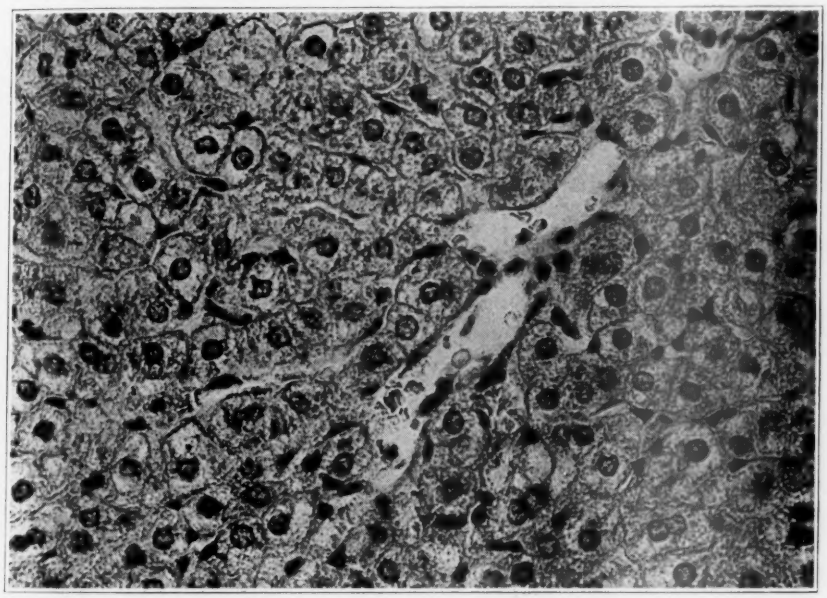

Fig. 7.—Liver three days after inoculation; × 360. The prominence of the Kupffer cells is striking. Clusters of histiocytic cells are common.

*Microscopic Examination of the Spleen.*—The earliest alterations in the spleen were hyperemia and increased erythrophagocytosis by the sinus endothelial cells. By from seventeen to twenty-four hours blood pigment was noted in appreciable quantities. The follicles, at first small, with little or no germinal centers, became definitely enlarged by from forty-eight to seventy-two hours. However, the most striking reaction during this period was the proliferation of the reticulum cells of the cords, which seemed to have produced pseudosecondary follicles. This activity gradually subsided, and by from fifteen to eighteen days germinal centers were rarely found and the erythrophagocytosis was normal in amount. In the one or two month specimens the follicles were large and the germinal centers pronounced. The proliferation of reticulum cells was not especially noticeable. In the one year specimen the follicles returned to normal size and the germinal centers were small.

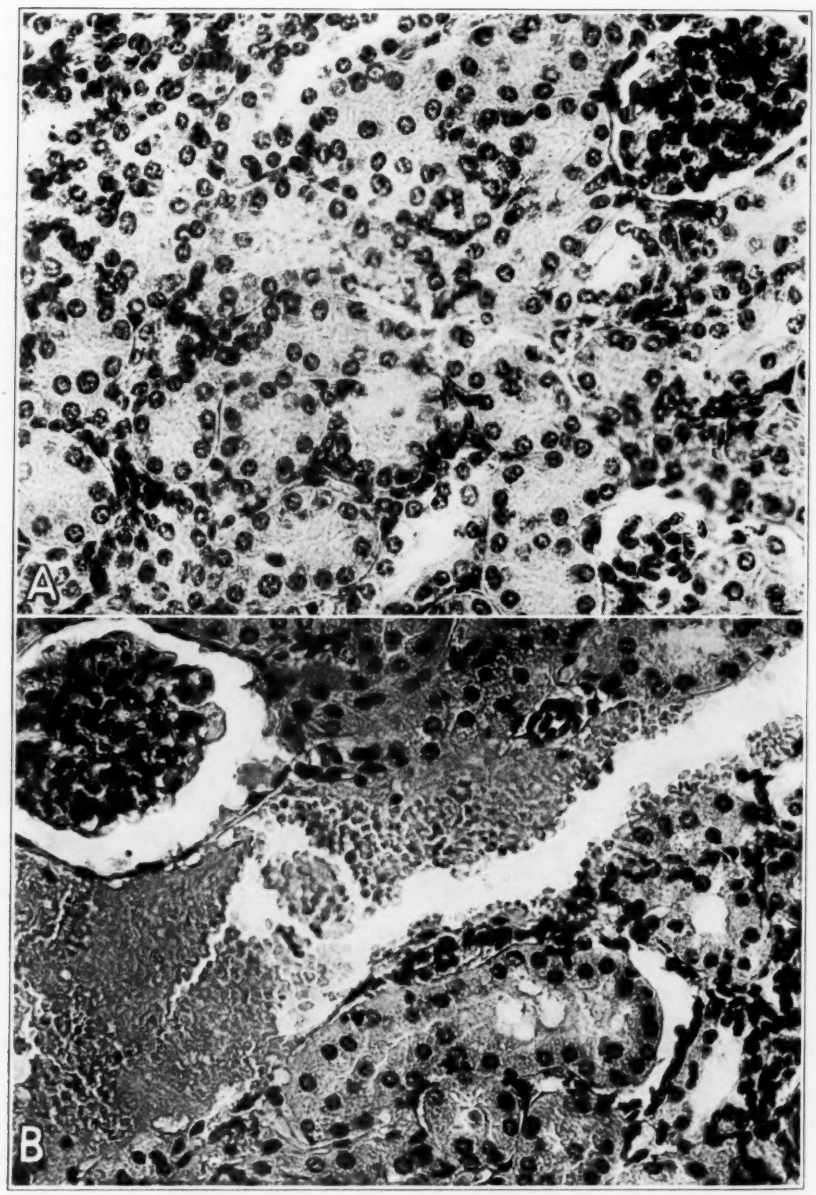


Fig. 8.—*A*, kidney three days after inoculation; × 360. The endothelial cells of the glomeruli are swollen. The interstitial tissue presents accumulations of proliferated histiocytes. *B*, kidney one year after inoculation; × 360. Note the large space filled with blood. The reaction to the tuberculin test was positive the day the animal was killed.

In the presence of a positive cutaneous reaction to tuberculin, marked hyperemia of the spleen and an increase in the blood pigment were observed.

*Microscopic Examination of the Lymph Nodes.*—Because a group of control animals of the same age living under similar conditions presented signs of intrapulmonary interstitial lymphocytic infiltrations and nodule formations, especially in the atelectatic subpleural areas, not dissimilar to those of the inoculated animals, the rôle of the lymph nodes could not be interpreted. It is true that in the eight day specimen huge secondary follicles were observed which almost resembled epithelioid tubercles (fig. 6*B*), but similar follicles were occasionally observed in a control animal. In addition, the state of the periaortic, the peritracheal and the mesenteric lymph nodes resembled that of the glands of the control animals.

The lymph nodes at the bifurcation of the aorta, especially at the site of inoculation, presented even more marked hyperplasia. The sinuses were wide; at first poor in cells, they were soon filled by large mononuclear phagocytosing cells, by lymphocytes and finally by pus cells. Acid-fast bodies, large and globoid, were found within the phagocytosing cells. Whether or not the latter bodies were related to tubercle bacilli could not be determined.

## HUMORAL OBSERVATIONS

*Blood.*—The alterations in the white blood corpuscles can best be understood from figures 9 to 12, inclusive. Therein are depicted the loss or gain in absolute numbers of polymorphonuclear leukocytes, monocytes and lymphocytes and the monocyte-lymphocyte (M/L) ratio. These graphs represent seventeen animals, of which three were control animals. (In another series, of sixteen animals, similar results were obtained.) The loss or gain was calculated from the average of one week's observations before inoculation, at least two readings for each animal having been made. The data for only three weeks are charted because after that time there was, except for occasional variations, a return to within the normal bounds. Studies of the blood, however, continued for one year.

In the graphs the unshaded circles represent the inoculated animals and the shaded circles the control animals. The interrupted lines bound the average control variations in loss or gain. Thus, the figures above the lines can be considered true gains or losses. This type of graphs was preferred to curves because of the marked variations that occurred in control animals of the same age living under identical conditions. One is aware that each animal reacts differently and thus must be its own control.

*Polymorphonuclear Leukocytes* (fig. 9).—An unquestionable rise in the number of these cells was manifest on the day of inoculation and reached its height by the second or the third day. A rapid return to within the range for the control animals occurred by the sixth day.

*Mononuclear Leukocytes* (fig. 10).—The interpretation of figure 10 is difficult. Discounting the control variations and considering the animals individually, one observed the following changes: a rise in the number of cells within the first twelve hours, a drop after the first day, another rise in two thirds of the cases on the third day, then a fall, followed by a third rise on the tenth day, and, finally, a return to within normal limits by the third week. If one considered the variations that occur in animals which have not been vaccinated, these changes in the monocytes are even more apparent. In a second series, of sixteen animals, the rise in the monocyte count at the end of the first week and the beginning of the second was more marked (the tuberculin test becomes positive in from seven to fourteen days).

*Lymphocytes* (fig. 11).—Compared with that of the control animals, the lymphocyte count remained within the normal bounds in the first three weeks of study. When one considered the animals individually, as many showed a rise as showed a fall.

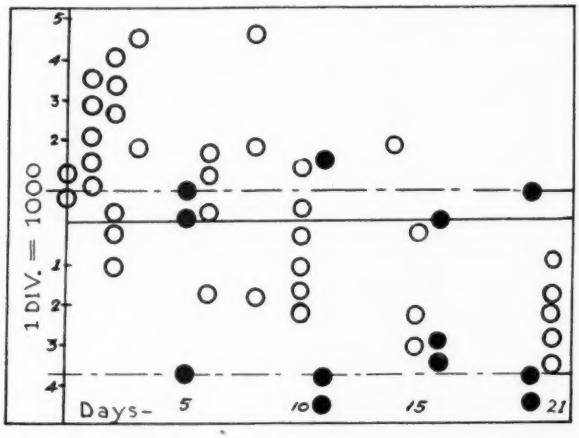


Fig. 9.—Graph showing the variation in the number of polymorphonuclear leukocytes. In this and the subsequent graphs, the black circles depict the controls, while the interrupted lines indicate the average normal variation. The representations are in terms of loss (below the base line) and gain (above the base line).

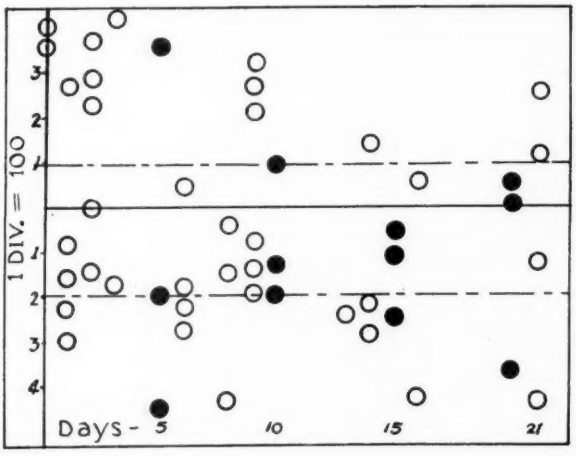


Fig. 10.—Graph showing the variations in the number of monocytes.

*Monocyte-Lymphocyte (M/L) Ratio* (fig. 12).—As the number of lymphocytes remained within normal bounds and the number of monocytes increased, the M/L ratio would naturally increase in a manner corresponding to the trend of the monocytes. This was the case in seven of the fourteen animals in the first seventeen days. By the third week the count returned to within normal limits.

*Sedimentation of the Erythrocytes* (fig. 13).—Figure 13 represents in millimeters the sedimentation rate of the erythrocytes calculated in terms of loss or gain from the normal for each animal. The data on twenty-two inoculated animals and three control animals are charted. Except in one case, in which a reaction took place at seventeen hours, there were no appreciable changes in the first forty-eight hours. On the third day, when the local lesion became fluctuant because of the formation of an abscess, the rate of sedimentation usually rose, although in

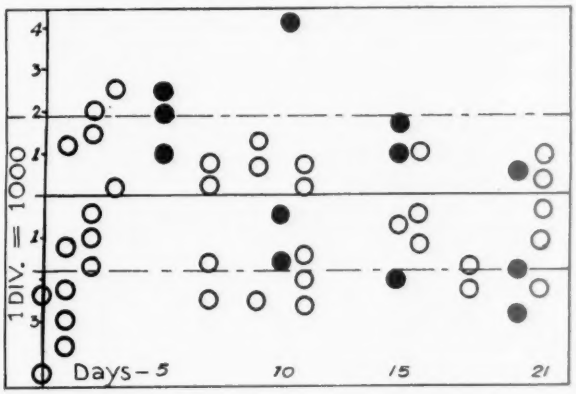


Fig. 11.—Graph showing the variations in the number of lymphocytes.

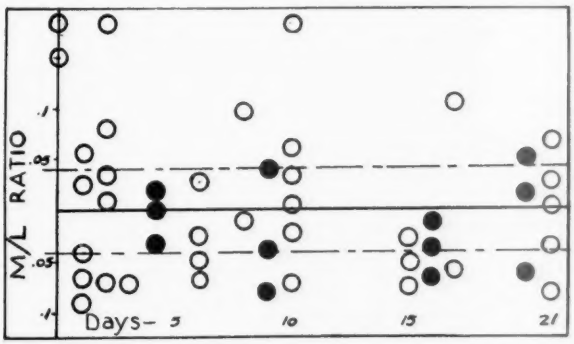


Fig. 12.—Graph showing the variations in the monocyte-lymphocyte ratio (M/L).

some cases only slightly. It remained exaggerated or returned to normal, depending on whether the abscess persisted or ruptured. By the second week, when as a rule signs of the abscess had disappeared in one way or another, the rate generally returned to within the normal limits. In one instance it became elevated in the third week. As the animal was not killed until some time later, the cause for this increase is not known. Not all the animals reacted with equal intensity. In one there was no increase, while in seven the increase was only within the normal range.

*Cells of the Abdominal Fluid* (table 1).—These cells varied from 3,200 to 21,500 per cubic millimeter in eleven animals. Examined at intervals from one hour to three weeks after the inoculation of BCG, the animals showed no appreciable change in the total number of cells.

The differential count was made by vital staining with neutral red followed by staining with Wright's method. Thirty inoculated animals and four control animals were thus studied. As shown in table 1, the absolute and the relative number of these cells did not differ during the entire experiment from those values for a control group. From 2 to 400 cells were counted in each case.

*Relation of the Tissue to the Humoral Response.*—Emphasis has been laid on the difficulty of interpreting the results of study of the blood because wide variations occurred in a group of control animals. However, changes did occur and could be correlated to alterations in the tissues.

The appearance in the local lesions of granulocytes in small numbers shortly after the injection of BCG and their gradual increase until they were numerous at two or three days almost exactly paralleled the change which took place in the

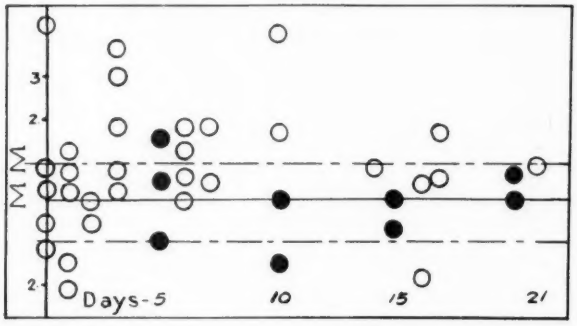


Fig. 13.—Graph showing the variations in the sedimentation rate of the erythrocytes.

TABLE 1.—*The Differential Count of the Cells of the Abdominal Fluid*

| | Inoculated Animal Differential Count, Percentage | | | | Control Animal Differential Count, Percentage | | | |
|---|---|---|---|---|---|---|---|---|
| | Monocytes | Lymphocytes | Eosinophils | Neutrophils | Monocytes | Lymphocytes | Eosinophils | Neutrophils |
| Before injection | 97 | 1 | 2 | 0 | | | | |
| After injection | 100 | 0 | 0 | 0 | | | | |
| 1 week | 83 | 7 | 10 | 0 | 93 | 2 | 5 | 0 |
| 3 weeks | 72 | 1 | 7 | 0 | 90 | 3 | 7 | 1 |
| 1 month | 96 | 0 | 4 | 0 | 97 | 1 | 1 | 1 |
| 2 months | 82 | 15 | 3 | 0 | 73 | 1 | 26 | 0 |
| 3 months | 88 | 2 | 10 | 0 | 92 | 2 | 6 | 0 |
| 4 months | 97 | 1 | 2 | 0 | 89 | 2 | 9 | 0 |
| 5 months | 98 | 0 | 2 | 0 | 93 | 2 | 5 | 0 |
| 6 months | 98 | 0 | 2 | 0 | 93 | 1 | 6 | 0 |
| 7 months | 84 | 7 | 3 | 6 | 94 | 3 | 1 | 0 |
| 8 months | 93 | 3 | 3 | 1 | 81 | 2 | 17 | 0 |
| 9 months | 92 | 7 | 1 | 0 | 86 | 1 | 3 | 0 |

blood. Then, depending on whether the pus was evacuated, or absorbed, a rapid or a slow decrease in the number of neutrophils occurred. After two weeks there was a uniform drop in the polymorphonuclear leukocyte count, and the site of inoculation was devoid of these cells.

The swelling of the septal cells of the lung, the Kupffer cells of the liver, the endothelial cells of the sinuses of the spleen, the glomerular capillaries, the reticulum cells of the spleen and the perivascular histiocytes, manifest in the earliest specimens examined (animals killed one hour and twenty minutes after inoculation), became more pronounced at from four to seventeen hours and corresponded to a rise in the number of monocytes in the blood. Histiocytes began to appear in the cutaneous lesion in small numbers at the same time. However, perivascular histiocytes with basophilia of their cytoplasm were found in increased numbers remote from this lesion. As the number of monocytes at the site of inoculation reached its height between the eighth and the tenth day, an increase in the number of monocytes occurred in less than half of the cases. Lymphocytes appeared at the lesion in small numbers, but no counterpart of this reaction could be observed in the blood.

## COMMENT

The results of these studies indicate that after the intradermal introduction of BCG there is not only a local response, with the formation of typical tubercles, but a generalized response, which is most pronounced in the lungs, liver, kidneys and spleen and is related to the reticuloendothelial system. The etiology of this response and its specificity remain to be explained.

Of cultures taken of the internal organs of thirty animals, one was positive. The method employed in the culturing of this tissue was the one practiced at the Pasteur Institute in Paris, namely, grinding the organs with sand, sterilizing with 5 per cent sulfuric acid, neutralizing and inoculating on various egg mediums (Löwenstein). Recently, Corper, using a similar method, found that he could recover 0.000001 mg. of tubercle bacilli.

Following the work of Fontes on the submicroscopic forms of the tubercle bacilli, the French school, led by Calmette and his co-workers [4] and Boquet, Nègre and Valtis,[15] showed that such forms can be recovered both in vivo and in vitro by serial inoculations. They were able to trace the entire life cycle of the organism in this manner. In a limited number of cases (table 2) serial inoculations were carried out with the organs of the animals of the aforementioned group. With one set of two animals positive cultures of the organs of the second were obtained despite the fact that cultures of the organs of the first were negative. In three other animals the reaction to the tuberculin test became positive after the intraperitoneal injection of a culture of organs that did not show tubercle bacilli. Similarly, in the results of experiments with two other groups of animals, one fed BCG orally and the other inoculated intravenously (Rosenthal [15a]), there was a strong

15. Boquet, A.; Nègre, L., and Valtis, J.: Compt. rend. Soc. de biol. **94**:235, 1926. Valtis, G.: ibid. **90**:19, 1924.

15a. Rosenthal, S. R.: Studies with BCG: II. Attempts at Dissociation and Increase of Virulence, Am. Rev. Tuberc. **35**:685, 1937.

indication that submicroscopic forms are diffused quickly by way of the lymphatics and the blood stream from the point of inoculation, thus accounting for the remote response of the reticulo-endothelial system.

Which fraction of the tubercle bacillus causes a stimulation of the reticulo-endothelial system? In an effort to answer this question the following experiments were performed:

Three week old cultures of BCG were dried, and acetone-soluble fractions and acetone-insoluble and methyl alcohol-soluble fractions were obtained (modified

TABLE 2.—*Observations Following the Intradermal Injection of BCG and Subsequent Intraperitoneal Inoculations of the Organs*

| First Group Inoculated | Second Group Inoculated | Interval Between Death and Inoculation, Days | Reaction to Tuberculin Test | Postmortem Smear of Local Lesion | Postmortem Smear of Organs | Postmortem Culture of Organs | Gross Pathologic Changes |
|---|---|---|---|---|---|---|---|
| 82 | .. | 1 | .. | + | — | — | Local hyperemia and pus cells; lymph nodes hyperemic |
| | 95 | 90 | — | .. | — | — | Negative |
| 94 | .. | 8 | — | + | — | — | Local abscess and enlarged lymph nodes |
| | 81 | 180 | — | .. | .. | — | Negative |
| | 88 | 180 | — | .. | .. | — | Negative |
| 128 | .. | 14 | + | + | — | — | Indurated local lesion and enlarged node |
| | 236 | 52 | — | — | — | — | Negative |
| | 242 | 52 | — | — | — | — | Negative |
| 134 | .. | 27 | + | — | — | — | Local 3 mm. scar; local lymph nodes enlarged |
| | 243 | 76 | — | .. | — | — | Negative |
| | 244 | 76 | — | .. | — | — | Negative |
| 68 | .. | 50 | + | — | — | — | Small scar at site of inoculation |
| | 89 | 150 | — | .. | .. | + | Negative |
| | 90 | 150 | — | .. | .. | + | Negative |
| 145 | .. | 73 | + | — | — | — | Negative |
| | 60 | 232 | + | .. | .. | — | Negative |
| | 54 | 232 | + | .. | .. | — | Negative |
| 93 | .. | 95 | + | — | — | — | Negative |
| | 191 | 216 | + | — | .. | — | Negative |

method of Boquet and Nègre.[16] Five milligrams (moist weight) of each fraction suspended in salt solution was injected intradermally into different animals. In addition, three other groups of animals were inoculated in a similar way with the following preparations: 0.2 cc. of a 1 to 10 dilution of old tuberculin, 0.1 cc. of concentrated old tuberculin and 0.0334 mg. of purified protein derivative.[17] In each group (except as otherwise indicated) the animals were killed after one day, one week and one month, and the local tissues as well as the internal organs were studied in a manner similar to that previously described.

16. This method differs from the original in that after the methyl alcohol extraction, the extract is passed through a Berkerfeld filter. The evaporation of the alcohol is done under pressure (40 pounds, or 18.1 Kg., at 60 C.).

17. The derivative used was prepared by the method of Seibert.

*Purified Protein Derivative (0.0334 Mg.).*—After one day the lungs presented moderate rounding of the septal cells, a seeming increase in their number and in some cases extrusion of the cells into the alveolar spaces. Within the capillaries mononuclear cells were also present, thus giving the lung the appearance of increased cellularity. At one week this cellularity was still in evidence, the intracapillary cells being less pronounced (fig. 14 *A*). The one month specimen revealed thin alveolar walls with a paucity of cells. The Kupffer cells of the liver presented increased phagocytosis and rounding in the one week specimen. The changes in the kidneys, spleen and lymph nodes were within normal limits.

The site of inoculation at one day disclosed a moderate infiltration of lymphocytes, polymorphonuclear leukocytes and swollen histiocytes in the cutis and the subcutis. Perivascular cellular accumulations were outstanding. By the end of the first week the process had practically abated, and the tissue had returned to normal by the end of the first month.

*Old Tuberculin (0.1 Cc. of the Concentrated Form).*—The observations almost duplicated those obtained with the protein derivative (fig. 14 *B*).

*Old Tuberculin (0.2 Cc. of a 1 to 10 Dilution).*—The six animals which received old tuberculin were killed one, two and seven days after inoculation. The lungs presented slight monocytic and polymorphonuclear intracapillary cellularity on the first day, followed by hyperemia on the second day (fig. 15 *A*). The one week specimen was entirely normal. The liver, too, showed intracapillary cellularity, which disappeared at one week.

The local lesion presented a fairly well localized area of cellularity in the cutis and the subcutis, which was mainly of histiocytic and lymphocytic origin. Granulocytes were sparse. Perivascular cellularity was prominent and even extended to the muscularis.

*Acetone-Insoluble and Methyl Alcohol-Soluble Fraction (Phospholipins).*—The lungs in the first week presented swelling and proliferation of septal cells (figs. 15 *B* and 16 *A*). Intracapillary lymphocytes and monocytes were present, but were less marked in the later specimen. The cellularity of these lungs was perhaps more marked than that of any others in the series. By the end of the first month they had reverted to normal (fig. 16 *B*). The Kupffer cells of the livers also participated in this activity, as evidenced by the increased phagocytosis and basophilia. The remaining organs (kidneys, spleen and lymph nodes) as far as could be detected histologically were normal.

The site of inoculation at the end of the first day was densely infiltrated with granulocytes, which extended throughout the reticular layer

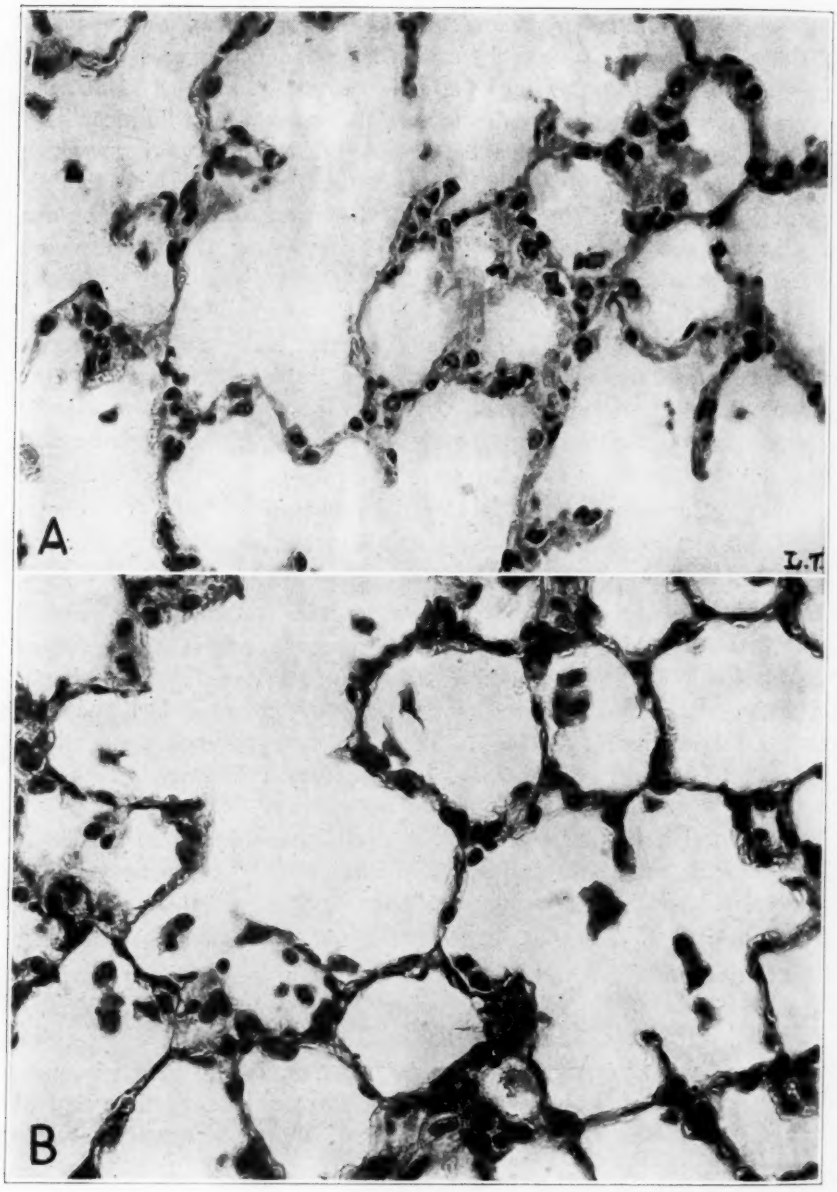


Fig. 14.—*A*, lung one week after the intradermal injection of purified protein derivative; × 360. Note the increased cellularity, the results mainly of swelling of the septal cells. *B*, lung one week after the intradermal injection of concentrated old tuberculin (0.1 cc.); × 360. The swollen and proliferated septal cells give the lung its cellular appearance.

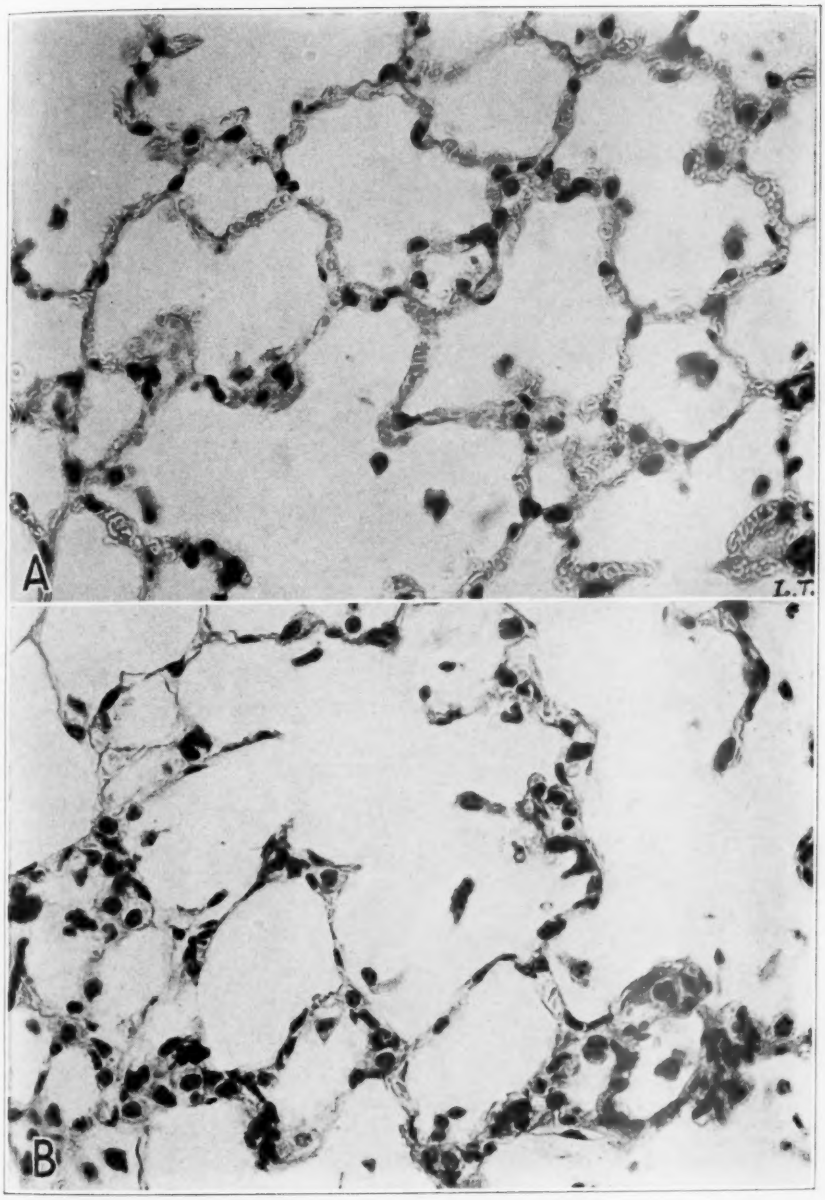


Fig. 15.—*A*, lung two days after the intradermal injection of dilute old tuberculin (0.2 cc. of a 1 to 10 dilution); × 360. The alveolar walls are slightly thickened as a result of capillary hyperemia. The septal cells show little or no reaction. Compare with 14 *B*. *B*, lung one day after the intradermal injection of phospholipins; × 360. Note the swollen septal cells. Compare with *A*.

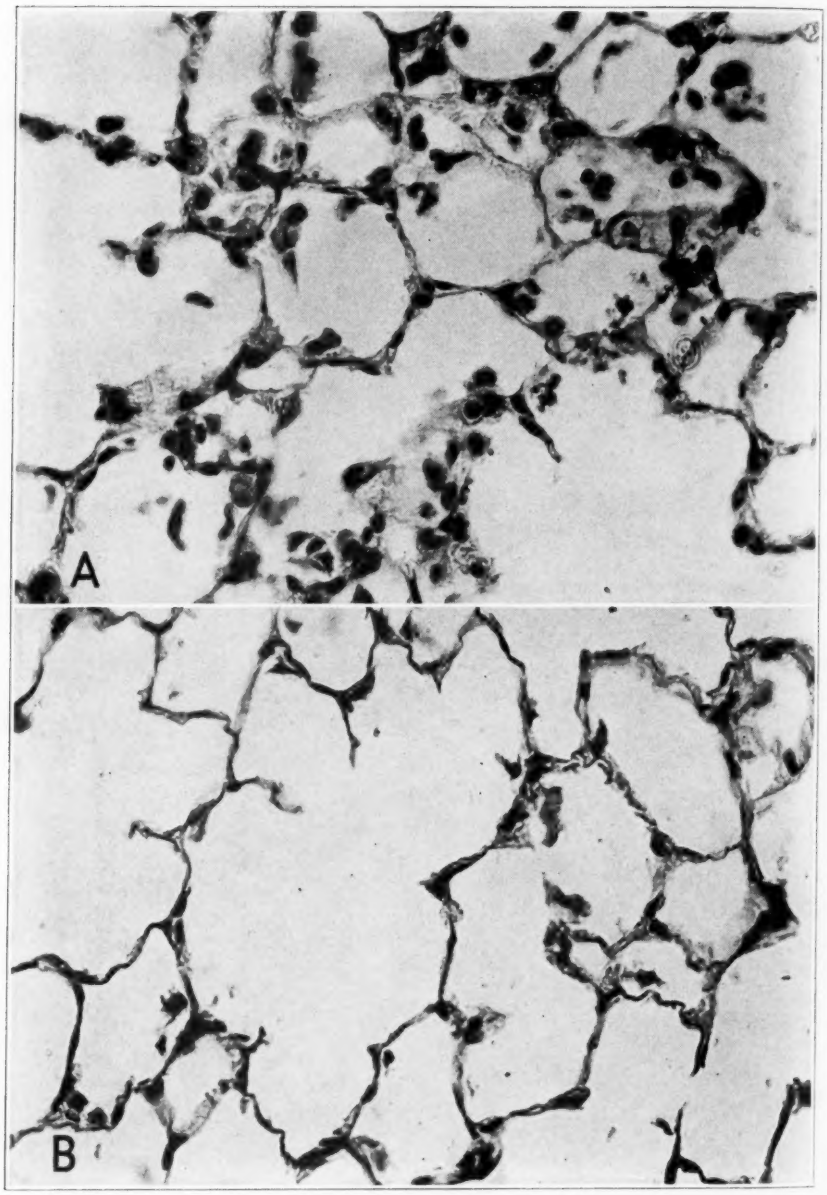


Fig. 16.—*A*, lung one week after the injection of phospholipins; × 360. The proliferations of septal cells have progressed. *B*, lung one month after the injection of phospholipins; × 360. The alveolar walls are thin and the septal cells pavement-like. Compare this section with the other sections of lungs.

of the cutis and the subcutis. Surrounding the lesion was marked perivascular cellularity, and there one also found proliferated histiocytes. The muscularis was included in this reaction. No acid-fast bodies were detected by the Ziehl-Neelsen method.

The one week specimen of the skin was difficult to cut. Thus, it is possible that a portion was dislodged in the process of cutting and staining. At the site of inoculation only histiocytes and lymphocytes were found, and there was perivascular cellularity remote from this lesion. After one month only slight cellularity remained, with some fibrosis.

*Acetone-Soluble Fraction.*—The reactions in these organs were similar to the ones described (fig. 17*A*) with the exception that in the local lesion of the animal killed one week after inoculation typical granuloma, composed of a central Langerhans giant cell surrounded by epithelioid cells and lymphocytes, was in evidence[18] (fig. 17*B*). Multinuclear giant cells of the foreign body type surrounded long yellow crystalline bodies. This formation was distinct from the granuloma. Acid-fast bodies could not be found with the Ziehl-Neelsen stain.

In summarizing, stimulation of the reticulo-endothelial system, as seen in the lungs and the liver, can be brought about by various fractions of the tubercle bacillus. It has been shown (Rosenthal[14]) that the introduction of trypan blue, the presence of parasites or pregnancy may be associated with a similar reaction. However, the response to these circumstances was in no instance as marked or as lasting as that observed after the introduction into the host of viable organisms. Although histologically the response of the reticulo-endothelial system was similar regardless of what foreign substance was introduced, this fact does not preclude an actual similarity because the injection of old tuberculin (0.2 cc. of a 1 to 10 dilution) into animals inoculated with BCG from fourteen days to one year previously called forth varying degrees of hyperemia (to the extent of hemorrhage) and activity of the reticulo-endothelial system in the internal organs and the granuloma, if present—a reaction without precedent in normal animals.

## SUMMARY

The intradermal introduction of BCG into guinea-pigs produced a local specific response, with the formation of tubercles, and a generalized nonspecific reaction of the reticulo-endothelial system. The latter reaction appeared soon after inoculation (one hour and twenty minutes), became definite at from one to three days, pronounced at from three to fourteen days and subsided by the third to the eighth week. In order of

18. This fraction was not passed through the Berkefeld filter.

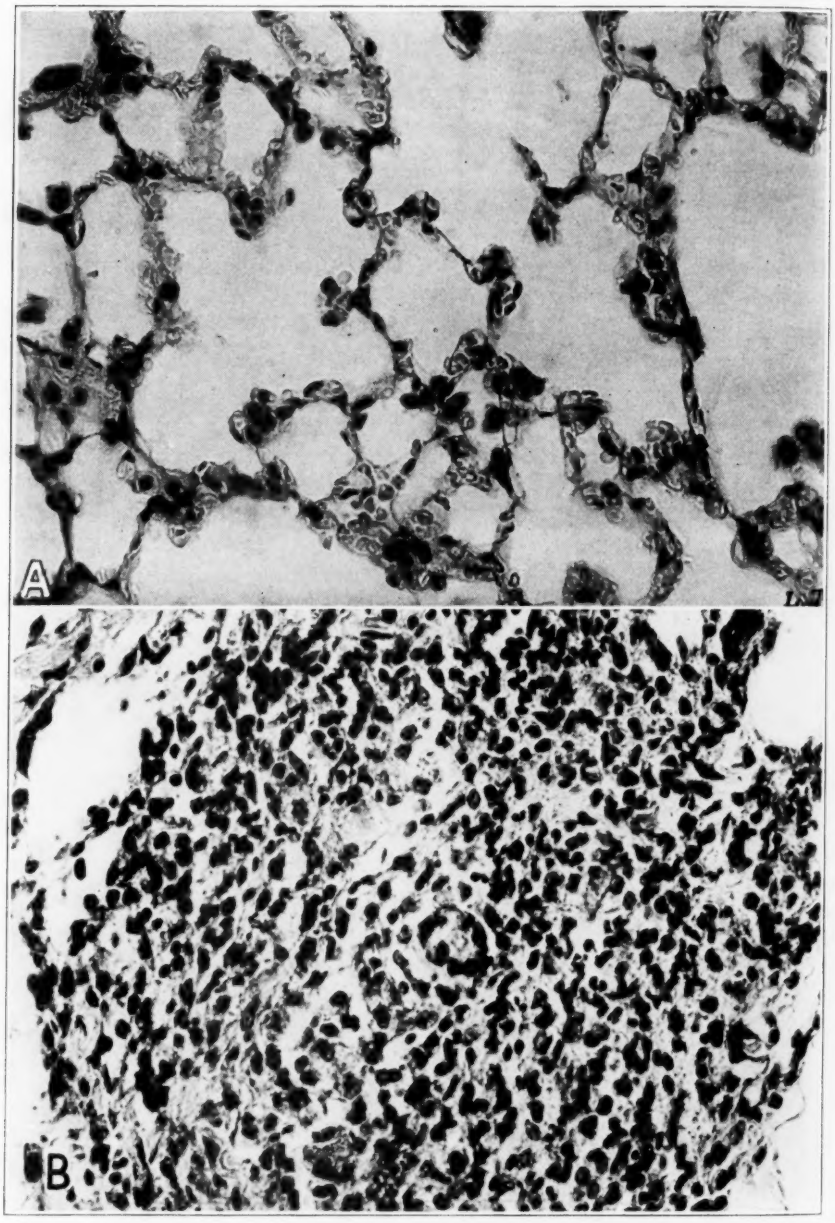


Fig. 17.—*A*, lung one day after the intradermal injection of acetone-soluble lipins; × 360. Note the hyperemia and the swelling of the septal cells. *B*, the local lesion one week after the injection of acetone-soluble lipins. A typical granuloma with a Langerhans giant cell is visible in the center.

intensity, the septal cells of the lung, the Kupffer cells of the liver and the reticuloendothelial cells of the spleen and the kidneys were affected.

A similar reaction of lesser intensity and shorter duration was observed following large intradermal doses of old tuberculin, purified protein derivative and acetone-soluble and acetone-insoluble and methyl alcohol-soluble fractions of BCG. Because other foreign substances (e. g., trypan blue and parasites) also stimulate the reticulo-endothelial system, it was deduced that this response was nonspecific from a histologic standpoint. However, in animals vaccinated with BCG (after fourteen days and until they were killed one year later) the intradermal introduction of old tuberculin (0.2 cc. of a 1 to 10 dilution) produced hyperemia and even hemorrhage in the internal organs and the granuloma, if present, as well as an increase in the activity of the reticulo-endothelial system, thus indicating some specificity.

The change in the number of polymorphonuclear leukocytes and monocytes in the blood, as well as in the sedimentation rate of the erythrocytes, paralleled the reactivity in the tissues. The cells of the abdominal fluid were not altered in number or in kind.

Serially injecting cultures of the internal organs of this group of animals into other animals revealed that viable BCG could be recovered from the latter although cultures of the organs of the former were not positive. Similarly, cultures of the organs of the second group produced positive reactions to the tuberculin test when injected into other animals. These results suggested the presence of submicroscopic forms and were thought to account for the stimulation of the reticulo-endothelial system.

# Case Reports

## SCLEREDEMA ADULTORUM (BUSCHKE), WITH INVOLVEMENT OF THE MUSCLES IN AN ELEVEN YEAR OLD BOY

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AND
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The similarity in the nomenclature and in the clinical symptoms of progressive indurations of the skin often makes their recognition difficult. In 1902 Buschke [1] described a progressive induration of the skin which differed from all other sclerodermatous processes in its clinical and more especially in its pathologic and prognostic aspects. He called it scleredema adultorum to differentiate it from similar conditions of the new-born. Since then more than fifty-four cases have been reported, mainly in German and in French, and scleredema adultorum has become recognized as a separate disease entity.

This form of scleredema is usually preceded by an infectious disease, such as angina, influenza, scarlet fever, erysipelas or a pyodermic infection of the skin. The deep cutis, the subcutis and occasionally the fascia and the muscles become indurated, hard and tight, causing limitation of motion in the affected parts. The progressive hardening usually begins in the face and the neck and involves the shoulders, the arms and the trunk and to some degree the lower extremities but not the hands and the feet. The prognosis is favorable as to recovery, though the disease may last from a few months to several years.

Most authors believe that the name scleredema adultorum is incorrect, since the condition has often been seen in infants and in children. Hoffmann [2] voiced the opinion that sclerema adultorum would be more proper. Sellei [3] suggested induratio progressiva benigna sub cute. Scleredema adultorum is apparently identical with the French *sclérème*

From the pediatric service of Dr. G. B. Bader, St. Vincent's Hospital.

1. Buschke, A.: Ueber Skleroedema, Berl. klin. Wchnschr. **39**:955 (Oct. 13) 1902.

2. Hoffmann, E.: Ueber Scleroedema (Scleremia) Adultorum nach Grippe mit Gewebsveränderungen an den cutanen Nerven, Klin. Wchnschr. **21**:963, 1923; Das Krankheitsbild des Skleroedema (Skleremia) adultorum (Buschke), Med. Klin. **11**:392, 1927.

3. Sellei, J.: Skleroedema adultorum (Buschke) (Induratio progressiva benigna sub cute), Dermat. Ztschr. **53**:161, 1928.

*des adultes* and possibly with acute generalized nonprogressive scleroderma, *sclérodermie generalisée*. However, the term scleredema adultorum is most commonly used.

The first and only contribution in the American literature on this condition was made in 1932 by Epstein,[4] who reported two cases and compiled forty-one cases previously reported. Only the more recent textbooks of dermatology mention the condition. No reference is made to it in the pediatric textbooks, although some twenty cases have been reported in children under 14.

The recent observation of scleredema adultorum in an 11 year old boy, the diagnostic problems encountered and the favorable course of the disease prompted us to report this case.

## REPORT OF CASE

H. F., a white boy 11 years old, born in the United States of Mexican parentage, entered the hospital on June 1, 1936. His complaints on admission were general weakness and swelling of the neck and the extremities. The family history was unimportant.

*History.*—His development was normal. He had measles, mumps, chickenpox and German measles. For the previous eight years he had had frequent nosebleeds. Tonsillectomy and adenoidectomy were performed when he was 5½ years old.

The present illness began about May 1, 1936, with chills, fever, malaise and sore throat. At the outset the child was treated in a city clinic, where he was given acetylsalicylic acid. When his condition did not improve a private physician was called, who made a diagnosis of Vincent's angina. At this time the child had some ulcerating lesions of the buccal mucosa. Neoarsphenamine was applied locally to the oral lesions, and small doses were given intravenously. Sodium perborate and hydrogen peroxide were then used locally. The oral lesions cleared up, but the general condition did not improve. Puffiness of the face, the neck and the arms was noticed, and the child was hospitalized.

*Examination.*—Examination revealed that the boy was well nourished, well developed, well oriented and cooperative but that he was acutely ill and showed extreme motor weakness. He was able to sit up alone for a few moments only with a great effort. He could stand, but he staggered when he attempted to walk. The scalp, the ears and the eyes, including the fundi, were normal. The mucous membranes of the mouth were clear. The tongue was coated but moist. The pharynx was slightly injected. The face appeared slightly puffed. The entire neck showed a peculiar swelling, which was most pronounced on the lateral aspects. There was no rigidity or pain on palpation. The consistency of the skin was not doughy, but a firm resistance could be felt in the subcutaneous tissues and muscles. There was no pitting on pressure. The skin was somewhat stretched, showing normal furrows and follicles. No glandular enlargement was present. The lungs were clear. The heart was not enlarged, and there were no murmurs. The heart sounds were muffled and of poor quality, and tachycardia was

4. Epstein, N. N.: Scleredema Adultorum (Buschke), J. A. M. A. **99**:820 (Sept. 3) 1932.

present, with a heart rate of 140. The liver and the spleen were not palpable. No abdominal tenderness or masses were present. On the parts of the extensor surfaces of the upper extremities, on the upper arms more than on the forearms, there was almost symmetrical, irregularly defined hard swelling. There was similar but less extensive swelling on the calves. The hands and the feet were not involved. The arms could not be fully extended either passively or actively without severe pain, though there was no tenderness on palpation. In appearance and consistency the skin in the involved areas was similar to that of the neck. The skin was only slightly depressible by means of prolonged strong pressure. There was no evidence of any inflammatory changes, and no eruptions were seen. The skin generally appeared waxy, yellow and dry.

Neurologic examination showed no evidence of involvement of the central nervous system.

Laboratory findings were as follows:

The Kahn test was negative on three occasions. The reactions to the Schick, the Dick and the tuberculin tests were negative.

A blood count on June 1 showed hemoglobin 70 per cent, red cells 5,090,000, white cells 12,200, polymorphonuclears 70 per cent, lymphocytes 21 per cent, monocytes 8 per cent and eosinophils 1 per cent. A count on June 6 showed hemoglobin 86 per cent, red cells 3,500,000, white cells 9,000, polymorphonuclears 78 per cent and lymphocytes 22 per cent. Sedimentation took place at the rate of 37 mm. an hour.

Chemical examination of the blood showed in milligrams per hundred cubic centimeters, sugar 87, nonprotein nitrogen 29.7, chlorides 474, cholesterol 140, albumin 3.6, globulin 2.3, phosphorus 5, calcium 9.2 and fibrin 0.49. The carbon dioxide-combining power was 60 volumes per cent.

A blood culture showed no growth in five days. A culture of material from the throat did not contain diphtheria bacilli. Unclassifiable pneumococci were observed by means of the inoculation of a mouse. A smear did not contain Vincent's organism.

The spinal fluid was clear, the pressure was not increased and the cell count was normal. No organisms were found on smear or culture. The colloidal gold curve was 1111100000; the total protein was 21.7 mg. and the sugar 56 mg. per hundred cubic centimeters.

The urine contained no sugar, albumin or casts. Occasional white cells and epithelial cells were observed. A twenty-four hour specimen contained 0.04 mg. of arsenic.

Examination of the muscles and the stools showed no evidence of trichinas.

The basal metabolic rate was plus 3.

A biopsy of skin and muscle from the left deltoid region was done on June 6. The histologic report of Dr. Alexander Fraser was as follows:

Skin: The epidermis was of normal structure but was considerably wrinkled. The bulges in the wrinkles were due to distention by fluid, whereas the depressions were caused by the resistance of the hair follicles, the arrectores pilorum and other nonelastic bands. The whole corium showed well marked intercellular edema widely separating the collagen fibers (fig. 1). These fibers were short, broken in places and curved or even curled. A specific stain for elastin was not made, but the picture of the corium, as described, was the same for all the ordinary stains. The cells were few, the number being approximately normal. The subcutaneous area of fat was fairly large but presented a normal appearance.

Musculature: The underlying muscle showed both intercellular and intracellular edema (fig. 2). The intercellular edema appeared as a clear space sur-

Fig. 1.—High power magnification of a section deep in the corium, showing the wide separation of all the fibers.

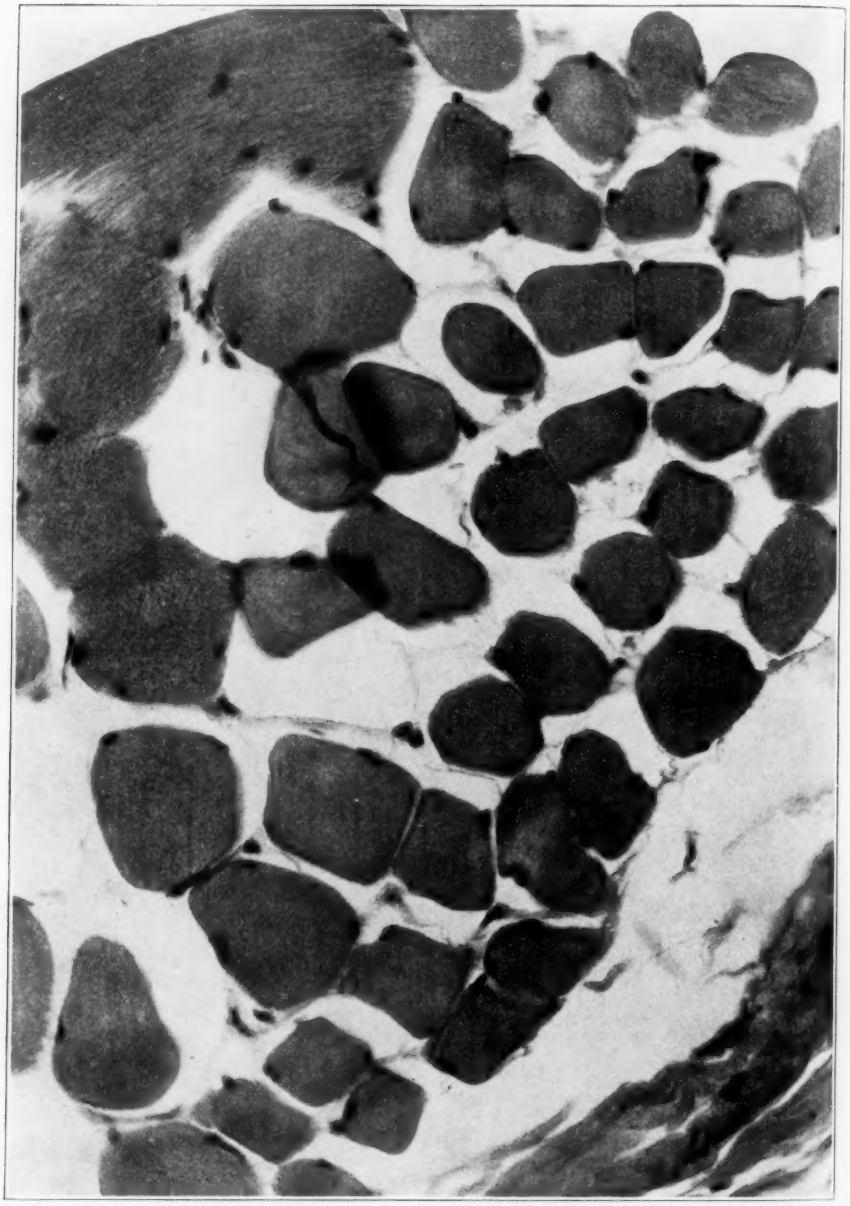

Fig. 2.—A section of muscle showing intercellular edema, characterized by small fibers surrounded by a wide clear space at the right and intracellular edema, characterized by large muscle fibers, at the left.

rounding the sarcolemma of the muscle fiber and apparently compressing the fiber, so that it appeared smaller than normal. The intracellular edema showed large fibers, half as large again as normal fibers. They were pinker than the yellowish, normal fibers when stained with hematoxylin and eosin stain. They were so distended in places that the membranes of the cells were fused, giving the appearance of a continuous sheet of muscle instead of distinct muscle fibers. The areas of distention showed clear spaces, probably representing fluid separating the myofibrillae so that they stood out distinctly. In a few places there was some atrophy of the muscle fibers, together with proliferation of the surrounding connective tissue. These areas were situated at the lower border of the musculature and appeared to have little significance.

*Further Course.*—The weakness and general malaise continued. The fulness of the neck increased, and the child began to have difficulty in swallowing. The temperature varied during the first ten days of hospitalization between 98.8 and 101 F., the pulse between 100 and 130 and the respirations between 20 and 30 per minute. On the ninth day a slight cough developed, and coarse râles were heard over the upper lobe of the right lung. The difficulty in swallowing and in breathing increased, and the child was able to take fluids only and those with the greatest effort. On the eleventh day he showed signs of consolidation over the upper lobe of the right lung. A diagnosis of aspiration pneumonia was made and was confirmed by roentgen examination. The child was critically ill; his temperature during the next five days varied between 104 and 105 F. and became normal by crisis. During the pneumonia the induration of the neck and the extremities began to subside, and it disappeared entirely when the temperature became normal. The child had a prolonged convalescence, gradually regaining strength and weight, and left the hospital six weeks after his admission. Examination on discharge failed to disclose any signs of muscular atrophy, contracture or pigmentary changes. The motion of the extremities was unrestricted and normal. Observation during the next six months revealed no changes.

### CLINICAL SYMPTOMS

In its typical form the disease is characterized by induration of the deep cutis, the subcutis and occasionally the fascia and the muscles, which gives a sensation of tightness and rigidity in the affected areas. The order of involvement is usually the nape of the neck, face, shoulders, arms, back and chest and to a lesser degree the lower extremities. The hands and the feet are almost always spared. The hardness and tightness bring on a varying degree of limitation in the motion of the extremities, head, neck and chest. A masklike facies has been observed, and often mastication, deglutition and respiration are difficult.

The skin appears pale and waxy, without any inflammatory changes. Occasionally the markings of the skin may be obliterated. The skin does not pit on pressure but may be folded slightly between the fingers.

In most cases the patient's general condition remains good. At the beginning of the disease confinement to bed may be necessary, especially when constitutional symptoms are present. Fever is usually

absent and when present is attributed to a coincidental disease. In a few cases a subfebrile temperature has been noticed.

Chemical examination of the blood and other laboratory examinations generally gave negative results. In some cases lymphocytosis is present. The duration varies from a few weeks or months to several years. In children it seems to be much shorter than in adults. The disease is more frequently seen in females than in males. The prognosis is favorable; a complete recovery without any sequelae is the rule, although remissions are frequent.

In the differential diagnosis scleroderma, dermatomyositis, trichiniasis, myxedema and Dercum's disease (adiposis dolorosa) are mentioned most frequently.

The distribution of the lesions, the consistency of the skin, the presence of pain and the general condition of the patient have been variously described by different authors. Finkelstein [5] saw in a 2½ month old girl swelling over the dorsum of the feet, lower part of the legs, thighs, genitals, buttocks and sacral region. The rest of the body was not involved. In the case of Buschke and Ollendorf [6] the lower parts of the legs were involved first, and the other portions of the body later. Kutter [7] found only the anal, genital and scapular regions involved, and Audry and Gradat,[8] the legs and thighs. Beck [9] observed indurations in the thighs and thought that only the fascia and the muscles had been affected. A type of swelling of the hands was described by Maschkilleisson and Abramowitsch [10] which did not hinder the motion of the fingers and hands.

The consistency of the skin has been described as waxy (Rummert [11] and Gruenmandel [12]), as velvety soft (Nobl,[13] von Graevenitz [14] and

5. Finkelstein, H.: Lehrbuch der Säuglingskrankheiten, Berlin, Julius Springer, 1924, p. 797.

6. Buschke, A., and Ollendorf, H.: Skleroedema adultorum mit muskulärer Lokalisation, Med. Klin. **23**:1406 (Sept.) 1927.

7. Kutter, P.: Skleremartige Hauterkrankung im Verlaufe einer encephalitischen Erkrankung bei einem Säugling, Ztschr. f. Kinderh. **36**:291, 1923.

8. Audry, C., and Gradat, J.: Sur le sclérème apronévrotique bénin (scléroedème de Buschke), Ann. de dermat. et syph. **1**:161 (Feb.) 1930.

9. Beck, J.: Skleroedema Adultorum Börgy, Urol. szemle **12**:307, 1927.

10. Maschkilleisson, L. N., and Abramowitsch, L. A.: Ueber Skleroedema adultorum (Buschke), Dermat. Ztschr. **72**:282 (Dec.) 1935.

11. Rummert, O.: Ein Beitrag zur Kenntnis des Skleroedema adultorum, Dermat. Wchnschr. **89**:1563 (Oct. 26) 1929.

12. Gruenmandel, cited by Rummert.[11]

13. Nobl, G.: Case Presentation, Arch. f. Dermat. u. Syph. **107**:440, 1911.

14. von Graevenitz: Ueber drei Fälle von Skleroedema adultorum (Buschke), Monatschr. f. Kinderh. **39**:257 (June) 1928.

Buschke [1]) and as boardlike hard (Seifert [15]). Other writers compared it to the consistency of paraffin before melting or to that of caoutchouc (india rubber). The absence of pitting has been emphasized by most authors, yet mention has been made that in some areas the skin is slightly depressible (*eindrueckbar*) (von Graevenitz,[14] Roscher,[16] and others).

In a few cases extreme weakness, malaise and loss of weight have been present, with severe subjective complaints (von Graevenitz[14] and Pinkus [17]). Pneumonia was present in Pinkus' [17] case. Severe pain was mentioned by Hoffmann,[2] Sellei,[3] Buschke,[6] Wiener [18] and others.

Transient eruptions have occasionally been observed in the involved areas, e. g., rose-colored erythema by Freund [19] and annular erythema by Blaschko.[20] Transient erythema preceded the condition in Epstein's [4] two cases. An unusual eruption was noticed by Maschkilleisson and Abramowitsch [10]; it was distributed symmetrically on the shoulders and consisted of linear lichenoid hyperkeratotic patches which involuted spontaneously with the improvement of the scleredema. Buschke [1] attributed the presence of an erythematous eruption in his first case to previous medication (with quinine and coal tar products).

### ETIOLOGY AND PATHOGENESIS

Little is known about the etiology of scleredema. An infectious origin is most likely, since in almost all cases the condition is preceded by an infectious disease. This view is supported by the fact that the induration of the skin frequently begins near the source of the infection and that scleredema has occasionally been observed in several members of the same family. Von Graevenitz [14] reported on two children in the same family who at about the same time suffered from it after pyoderma. Bamberger [21] described it in a mother whose three children showed various degrees of thickening of the skin of the legs and the face; presumably one had scleredema. Various bacteria or their toxins apparently may produce the same clinical syndrome. In the cases so far reported cultures of the blood were negative, as were cultures of the subcutis (Hoffmann [2]).

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15. Seifert, A.: Skleroedem bei einem 6 Jahre alten Kinde, Arch. f. Kinderh. **91**:220, 1930.

16. Roscher, cited by Rummert.[11]

17. Pinkus, F.: Zwei Fälle von Skleroedem, Dermat. Ztschr. **14**:425, 1907.

18. Wiener: Skleroedem und Zungenveränderungen im Verlaufe eines Falles von perniziöser Anämie, Zentralbl. f. Haut.- u. Geschlechtskr. **17**:269, 1925.

19. Freund, H.: Ueber Skleroedem (Buschke). Unter besonderen Berücksichtigung der Histologie, Arch. Dermat. u. Syph. **161**:92, 1930.

20. Blaschko, cited by Rummert.[11]

21. Bamberger, E., cited by Rummert.[11]

Other authors have suggested a disturbance in the function of the glands of internal secretion as the cause of scleredema. Dysfunction of the thyroid gland is believed by many to be a contributory cause owing to the resemblance of the clinical findings and, especially, of the histopathologic observations to those in cases of atypical myxedema. Both hyperthyroidism and hypothyroidism and disturbances in the function of the pituitary and the ovarian glands have been observed, although substitution therapy was of no avail. Hoffmann [2] considered a causal relationship with the vegetative nervous system, basing his idea on his histologic observations on the cutaneous nerves.

One can only speculate about the pathogenesis. The edema described has been compared to myxedema and is much unlike the edema of cardiorenal origin. According to Rummert [11] there is no accumulation of fluid between the elements of the tissue and such fluid cannot be demonstrated through scarification or histopathologic examination. Some writers suggest a lymph block or an elephantiasis-like process as the pathomechanism of the indurations in the involved tissues. Freund,[19] who carried out exhaustive studies regarding the histopathologic picture of these diseases, was able to observe, with special staining methods, an amorphous substance between the hollow spaces of the connective tissue bundles, the exact chemical nature of which he was unable to identify. He expressed the opinion that the substance was mucin-like, though a staining for mucin was not conclusive. Weidman [22] observed that in some cases the material was more amyloid in its microchemical reactions.

The origin of this amorphous substance is unknown. Some authors believe that it is an exudate and the product of the fibroblasts rather than the result of thyroid dysfunction. Definite changes in the endocrine glands have been present in only a few cases (Seifert,[15] Freund [19] and Rummert [11]) and the possibility of dysfunction in many. Therefore, it is possible that an infectious process causes dysfunction in the glands of internal secretion which result in alterations of the integument. There have been no postmortem observations which could substantiate this view.

## PATHOLOGY

The histopathologic observations have not been uniform in all the reported cases. In most cases no great changes are seen in the epidermis. The keratohyaline layer and the stratum corneum are normal; the rete pegs are usually well preserved, though in some areas they are more thickened and in others more flattened. Moderate pigmentation may be seen in the basal cells. The papillary layer is normal. In the upper layers of the cutis propria there is an occasional perivascular

22. Weidman, Fred D., in discussion on Epstein.[4]

infiltration consisting of round cells, connective tissue cells, plasma cells and a few mast cells. In the deeper layers of the cutis and the subcutis there is a peculiar edematous space, with blank gaps around the blood vessels and the epithelial appendages, which separates the connective tissue fibers. The collagen bundles appear greatly swollen and edematous.

In some cases a faintly stainable mass is found in the blank spaces, which also penetrates the collagen fibers. This is supposed to be a mucin-like substance and can be shown only with special stains. The elastic fibers are usually normal but may be short or torn in the presence of extensive edema. The blood vessels may be widely dilated and filled with blood. Occasionally the walls of a vessel are greatly thickened. The lymphatic vessels are also dilated. The smooth muscles are more or less hyperplastic. In one case the cutaneous nerves were thickened, wavy and swollen, with a perineuritic infiltration (Hoffmann [2]).

Reports on the pathologic changes in the muscles are scarce. In the case of Buschke and Ollendorf [6] the muscle fibers were described as separated by an amorphous substance without evidence of any inflammatory infiltration. Most of the muscle fibers were well preserved and showed no necrosis or waxy degeneration.

## THERAPY

No specific therapy is known, and the treatment has been mostly symptomatic. Improvements and recoveries have been described following the use of salicylates, iodides, hot baths and massages. Some authors have reported a beneficial response to the administration of various glandular products, such as thyroid, hypophysial and ovarian extracts, while others failed to observe any improvement from the use of these products. The evaluation of any therapeutic measure is difficult in the case of a disease from which spontaneous recovery is common. Recovery may be hastened, however, by means of the aforementioned therapeutic measures.

## COMMENT

The meager reports on scleredema in the English literature give the impression that the disease is nonexistent in the English-speaking countries. It is more likely that in many cases of scleredema in which recovery followed a relatively mild course the condition was diagnosed as acute scleroderma. This is especially true with regard to infants and children because a biopsy to verify the diagnosis is not resorted to as often for them as it is for adults. The favorable prognosis in cases of scleredema makes recognition of the disease desirable, yet a definite

diagnosis is arrived at in some cases only after complete involution has occurred without evidence of atrophy, contractures or pigmentation.

The main characteristics of scleredema were present in our case; i. e., the condition followed an infectious disease, there was typical induration in the usual locations and a complete recovery followed. The histopathologic observations confirmed the diagnosis. There was simultaneous involvement of the muscles, beyond a doubt, as is well demonstrated in figure 2. The unusual feature in our case was the complicating pneumonia, which was apparently caused by the extensive involvement of the muscles of mastication and deglutition. The brief course and the rapid involution following pneumonia may have been aided by the presence of high fever during the pneumonia. The effect of fever was also noticed by Maschkilleisson and Abramowitsch,[10] in whose case a definite improvement was noted after recurrent erysipelas.

In many of the reported cases the condition was at first believed to be diffuse scleroderma because the distribution, the clinical appearance of the induration and the limitation of motion of the affected parts were similar to those phases of diffuse scleroderma. This diagnosis was not considered in our case since involvement of the hands and the feet, usually present in the early stages of scleroderma, was absent. The motion of the hands, fingers and feet remained free throughout the course. Discoloration of the skin, erythematous pigmentary changes and the ivory-yellowish infiltrations frequently seen in scleroderma were also absent.

The only other possible diagnosis which could have been considered was dermatomyositis. The marked weakness, fever, tachycardia, pain and pneumonia are more constant symptoms of dermatomyositis but have likewise been observed in cases of scleredema. Cutaneous eruptions, such as erythema, urticaria, purpura and pemphigoid lesions, which are practically always present in dermatomyositis, were absent in this case. The histopathologic diagnosis of dermatomyositis was excluded by all the pathologists who examined the slides, since no inflammatory changes (the presence of mononuclear and polymorphonuclear leukocytes, hemorrhages, necrosis and various forms of degeneration of the muscle fibers) such as those described by Steiner,[23] Friedman,[24] Karelitz [25] and others were present. The brief course and the complete recovery without atrophy, contractures, fibroses or calcifications speak against a diagnosis of dermatomyositis. This fact is

23. Steiner, W. R.: Dermatomyositis, with Report of Two Cases, J. A. M. A. **76**:271 (Jan. 28) 1922; Dermatomyositis, in Osler, William: Modern Medicine, Philadelphia, Lea & Febiger, 1927, vol. 5, p. 784.

24. Friedman, E. D.: Dermatomyositis, M. J. & Rec. **123**:382, 1926.

25. Karelitz, S., and Welt, S. K.: Dermatomyositis, Am. J. Dis. Child. **43**: 1134 (May) 1932.

important if one considers the grave prognosis and the high mortality rate recorded for dermatomyositis in children; according to Karelitz,[25] in eighteen cases reported seven patients died and the remaining eleven showed some atrophy, contractures or other sequelae.

The involvement of the muscles in our case simulated that of trichiniasis to some degree. However, there was no history of gastrointestinal disturbance, and the search for trichinas in the muscles and the stools gave negative results. The absence of eosinophils in the blood and the course of the disease definitely excluded the possibility of trichiniasis.

## SUMMARY AND CONCLUSIONS

A case of scleredema adultorum (Buschke) following an infectious disease (Vincent's angina or stomatitis) in an 11 year old boy is reported, and the literature is reviewed with especial reference to infants and children. This disease was of a mixed type, affecting the integument and the muscles, with consecutive limitation of motion of the head, the neck and the extremities, and was complicated by aspiration pneumonia apparently due to the involvement of the muscles of mastication and deglutition. Complete recovery took place within six weeks after the pneumonia.

Scleredema is undoubtedly a separate disease entity, the recognition of which is important because of the favorable prognosis. The clinical resemblance to acute scleroderma and especially to dermatomyositis in our case is admitted. A histopathologic examination is essential in the differential diagnosis in some cases. The presence of fever in our case appeared to alleviate the disease, but one cannot say definitely that it did without further study.

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# LAURENCE-MOON-BIEDL SYNDROME

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The syndrome comprising obesity, hypogenitalism, mental deficiency, polydactylism and pigmentary disturbance of the retina was first described seventy-three years ago by Laurence and Moon.[1] Although they intimated that this peculiar combination of clinical signs might be more than fortuitous, the fact was not fully appreciated until comparatively recent times that its various components make up a unit syndrome and that its familial character is of fundamental significance. Because Biedl [2] placed appropriate emphasis on the significance of these factors, he has come to share with the original authors the title by which this condition is now commonly known.

It is noteworthy that this clinical picture has attracted the greatest attention from ophthalmologists and from students of endocrinology. The pediatric literature, wherein the condition should have found frequent mention, has contained relatively scant reference to it. Likewise, it is interesting to note that until recently most of the case reports and discussions appeared in foreign journals. The first description of the syndrome in this country was published in 1925 by Solis-Cohen and Weiss.[3] Several case reports have recently appeared in American pediatric journals.[4]

Before I present a detailed description of several cases of this condition in one family, with which I have come into contact, it will be profitable to comment briefly on its most important features. A more detailed consideration may be found in the excellent reviews on the subject by Reilly and Lisser [5] and Cockayne, Krestin and Sorsby.[6]

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From the Northern Michigan Children's Clinic, Marquette, Mich.

1. Laurence, J. Z., and Moon, R. C.: Brit. Ophth. Rev. **2**:32, 1866.

2. Biedl, A.: Deutsche med. Wchnschr. **48**:1630, 1922.

3. Solis-Cohen, S., and Weiss, E.: Dystrophia Adiposogenitalis, with Atypical Retinitis Pigmentosa and Mental Deficiency—the Laurence-Biedl Syndrome, Am. J. M. Sc. **169**:489, 1925.

4. Jenkins, R. L., and Poncher, H. G.: Pathogenesis of the Laurence-Biedl Syndrome, Am. J. Dis. Child. **50**:178 (July) 1935. Arena, J. M.: Laurence-Moon-Biedl Syndrome, J. Pediat. **10**:62, 1937.

5. Reilly, W. A., and Lisser, H.: Laurence-Moon-Biedl Syndrome, Endocrinology **16**:337, 1932.

6. Cockayne, E. A.: Krestin, D., and Sorsby, A.: Obesity, Hypogenitalism, Mental Retardation, Polydactyly, and Retinal Pigmentation: The Laurence-Moon-Biedl Syndrome, Quart. J. Med. **4**:93, 1935.

Until 1932, only twenty-five instances of the complete syndrome were reported.[5] In addition, ten cases in which the syndrome could be considered questionably complete, twenty-seven representing the incomplete form and fifteen questionable examples were reported. Judging by the accelerated frequency with which this condition has been recognized in the past five years, its incidence is undoubtedly greater than the reported statistics lead one to believe.

The field of pathology has been barren in its contributions toward an understanding of the etiology of this condition. Both the hypophysis and the hypothalamus have been implicated by some authors without substantiation. The familial factor, however, is such an outstanding feature that in considering the pathogenesis of the syndrome it is difficult to understand why until recently the genetic aspects failed to receive more attention. From this point of view the most acceptable concept, recently set forth, is that the condition results from a hereditary developmental disturbance and that the various parts of the syndrome represent mesoblastic (polydactylism) and epiblastic (obesity, retinitis pigmentosa, mental inferiority and genital dystrophy) defects which are recessive and due to mutations of two genes in the same chromosome.[7]

Visual disturbance is noted early in life, although occasionally it does not make its appearance until the age of 5 years or later. Although retinal degeneration is a constant finding, the character of the pigmentary disturbance varies greatly. The "bone corpuscle" pigmentary changes along the retinal vessels at the periphery, characteristic of typical retinitis pigmentosa, are infrequently seen, and atypical forms are far more common.

Polydactylism, an anomaly seen also in persons not affected by the syndrome, presents interesting variations. It may be present in one or all extremities, occurring symmetrically or asymmetrically. It may vary in location and in structural type. More than one extra digit on an extremity has not been reported. The extra digit is always toward the little toe or finger (postaxial) and varies from a small fibrous nodule, with or without contained bone structure, to a duplication of a digit. The absence of polydactylism accounts for many instances of the incomplete form of the syndrome. Syndactylism may be present as an additional anomaly or may occur in the absence of supernumerary digits.

In most instances, mental inferiority is apparent early and appears as a developmental defect. Infrequently, it develops later in a child whose mental progress has been normal. While mental retardation is rarely absent, the deficiency is occasionally mild.

7. Jenkins and Poncher.[4] Cockayne, Krestin and Sorsby.[6]

So far as genital hypoplasia is concerned, uncertainty frequently arises as to both its presence and its degree. This is particularly true with girls and in the period before secondary sex changes take place. Instances, however, have been reported in which hypogenitalism was definitely absent.

A number of associated conditions have been observed, among them nystagmus, strabismus, deafness, shortness of stature, deformities of the skull, abnormal shortness of the hands and the feet, irregularity of the toes, genu valgum, bilateral coxa vara, scoliosis, deformities of the skull, congenital heart disease and anal atresia.

The differential diagnosis offers no great difficulties except possibly in the case of the juvenile form of amaurotic family idiocy, as described by Vogt,[8] Spielmeyer,[9] Sjögren [10] and others, in which the funduscope reveals pigmentary abnormalities often indistinguishable from those found in the Laurence-Moon-Biedl syndrome. This disease also has definite hereditary features, but it is to be emphasized that its signs appear gradually at about the age of 5 years in children who have been developing normally. Mental inferiority in cases of the Laurence-Moon-Biedl syndrome is usually apparent in infancy. Other significant differences exist. Juvenile amaurotic idiocy is more rapidly progressive, ending with death between the ages of about 14 and 16 years. Besides a steady loss of intelligence, the subject exhibits progressive motor weakness, culminating in complete spastic or flaccid paralysis, usually in the form of diplegia, a clinical picture indicative of progressive involvement of the upper motor neurons. In contrast, the Laurence-Moon-Biedl syndrome is "neurologically silent."

## DESCRIPTION OF A FAMILY

The family reported on was of French-Canadian origin. The mother and father were both living. The former was obese, and the latter had chronic arthritis. Obesity occurred frequently on the father's side. The family history is of special interest because of the frequency of twinning, this hereditary tendency having originated on the paternal side. A total of sixteen instances of twinning were traced through three generations.

Thirteen children were born to the parents of the family under discussion, eight of whom were living. Premature twins, resulting from the second pregnancy,

8. Vogt, H.: Ueber familiär amaurotische Idiotic und verwandte Krankheitsbilder, Monatschr. f. Psychiat. u. Neurol. **18**:161 and 310, 1905; Zur Pathologie und pathologischen Anatomie der verschiedenen Idiotie-Formen, ibid. **22**:403 and 490, 1907; **24**:106, 1908.

9. Spielmeyer, W., and Nissl, F.: Histologische und histopathologische Arbeiten über die Grosshirnrinde mit besonderer Berücksichtigung der pathologischen Anatomie der Geisteskrankheiten, Jena, Gustav Fischer, 1908, vol. 2, p. 193.

10. Sjögren, T. S.: Die juvenile amourotische Idiotie, Hereditas **14**:197, 1931.

died soon after birth. The fourth child, a girl (M. M.), died at the age of 12 years, the cause of death not being clearly understood. She had six toes on each foot and six fingers on each hand (fig. 1). Poor vision and Fröhlich's type of obesity were also present. The status of her intelligence was not determined. The eighth child, a boy, died at the age of 13 months of a pulmonary infection. He weighed 11½ pounds (5,216 Gm.) at birth and was obese until death. He had six toes on the right foot and six fingers on each hand. The twelfth child, a girl, died at the age of 3 days, the cause being unknown. She weighed 11 pounds

Fig. 1.—M. M., who died at the age of 12 years, the cause being unknown (the photograph was supplied by the parents). Obesity, visual disturbance and polydactylism were present.

(4,989 Gm.) at birth and had loosely attached to the right little finger a supernumerary appendage, which was easily amputated.

Of the eight living children, six were apparently normal and had none of the cardinal signs of this syndrome. The remaining two children were considered affected.

Case 1.—V. M., the ninth child, a boy, was first seen at the clinic on May 1, 1934, at the age of 11 years, because of obesity and poor vision. He was born at

full term, weighing 8½ pounds (3,855 Gm.). He had always been overweight. At the age of 1 year he weighed 30 pounds (13.6 Kg.) and at 2 years 55 pounds (24.9 Kg.). He was nursed for fifteen months. Outside of an occasional infection of the upper respiratory tract and measles, he had no illnesses. Failure of vision had been slowly progressive from the age of 5 years. During the last few years he had been having considerable difficulty in getting about at night, often stumbling over objects.

*Physical Findings.*—The boy was obviously below par mentally. Psychometric examination revealed feeblemindedness, with the rating of a moron and an intel-

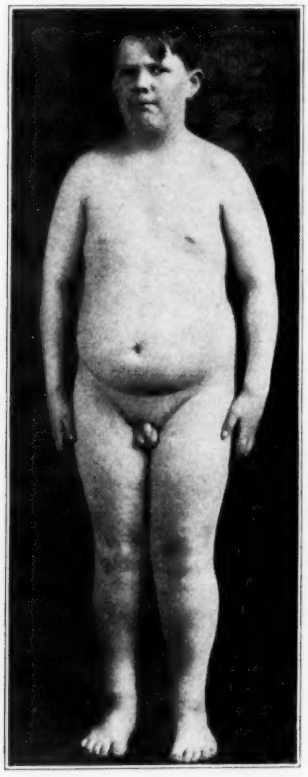

Fig. 2 (case 1).—Patient V. M. at the age of 13 years. Obesity, retinitis pigmentosa, mental retardation and rudimentary polydactylism were present. The external genitalia were fairly well developed.

ligence quotient of 66. He was 56 inches (142 cm.) in height, which is within the average limits for his age. He had a type of obesity corresponding with that usually ascribed to dystrophia adiposogenitalis (fig. 2). Adiposity was pronounced in the proximal parts of the extremities, over the lower part of the abdomen and in the region of the breasts. The patient had a moderately short, thick neck. His skin was smooth and warm. There was no enlargement of the thyroid. When he was first seen, his external genitalia appeared smaller than normal for his age,

but when he was reexamined sixteen months later, they appeared normally developed. During that interval, however, he had received treatment with thyroid and pituitary extracts. He had mild genu valgum and moderate relaxation of the plantar arches. There was slight tapering of the fingers. At the lateral aspect of the base of the right little finger a small skin-covered fibrous nodule without a bony center was present (fig. 3). Examination of the eyes showed considerable reduction of vision. The child could distinguish the examiner's fingers at 4 feet (122 cm.) on the right and at 9 feet (277 cm.) on the left. Alternating divergent strabismus was present bilaterally. The visual fields were constricted, especially in the superior portions. Fundoscopic examination revealed a myopic astigmatic type of fundus. The disks were of normal color, with no evidence of cupping or choking. The retinal vessels were attenuated, and in the peripheral part of the retinas there was pigmentary stippling, but not of the "bone corpuscle" type. Atrophic retinal

Fig. 3 (case 1).—Photograph of V. M.'s hand, showing rudimentary polydactylism at the base of the right little finger, represented by a fibrous nodule.

changes were especially evident in the periphery. The impression of the fundoscopic picture was that of pigmentary degeneration of the retina, compatible with a diagnosis of retinitis pigmentosa. The remainder of the examination showed nothing abnormal outside of dental caries, evidence of poor oral hygiene and deviation of the nasal septum.

*Laboratory Data.*—A Kahn test of the blood and an intracutaneous tuberculin test gave negative results. The blood cholesterol content was 180 mg. per hundred cubic centimeters. The carbon dioxide-combining power of the blood was 63 volumes per cent. The basal metabolic rate was minus 23 per cent on May 2, 1934, and minus 21 per cent on Oct. 31, 1934.

*Roentgenologic Studies.*—Roentgen films of the skull and the pituitary fossa did not reveal any definite abnormalities. Studies of the wrists showed no evidence of delayed development.

*Treatment.*—The patient was placed on a reduction diet of 1,200 calories and was given thyroid extract. As a result, he lost approximately 15 pounds (6.8 Kg.). At the end of six months he had lost 30 pounds (13.6 Kg.). Thereafter his weight fluctuated in relation to periods of relaxation of dietary restrictions and omission of thyroid extract. His visual difficulties increased somewhat.

CASE 2.—E. M., the thirteenth child, a girl, was first seen at the age of 22 months, referred by the family physician because of obesity. She was a full term baby, weighing 10½ pounds (4,763 Gm.) at birth. At the time of her first visit

Fig. 4 (case 2).—Patient E. M. at the age of 2 years. Obesity, mental retardation, polydactylism and ptosis of the right upper lid were present.

to the clinic, she had just begun to walk with support but had not yet begun to talk. All her deciduous teeth had erupted. Ptosis of the left upper eyelid, associated with facial asymmetry on the same side, was noted soon after birth. After the age of 1 year she had several attacks of hyperpyrexia, associated with pyuria.

*Physical Findings.*—The patient was a large, obese baby showing evidence of submental development. She weighed 42 pounds (19.1 Kg.). Her obesity was similar in type to that of her brother (case 1), with the greatest distribution of fat over the abdomen and in the shoulder and the pelvic girdle (fig. 4). A super-

numerary toe was found arising from the midportion of the medial aspect of the right little toe (fig. 5*A*). A small fibrous nodule was noted at the base and the lateral aspect of the right little finger (fig. 5*B*), identical in appearance and location with the nodule observed in the case of her brother (fig. 3). Ptosis of the left upper lid and suggestive flattening of the left side of the face were present, but there was no inability to close the left eye. Fundoscopic examination revealed normal fundi, although a heavy ring of pigment around the right disk, which was not considered pathologic, was noted. No visual disturbances were as yet demonstrable. A general physical examination revealed no other abnormalities outside of large septic tonsils and a dime-sized round pigmented area in the left inguinal region.

Routine examinations of the urine and the blood gave negative results, as did a Kahn test of the blood and an intracutaneous tuberculin test. Roentgenologic studies of the pituitary fossa and the wrists showed no definite abnormalities.

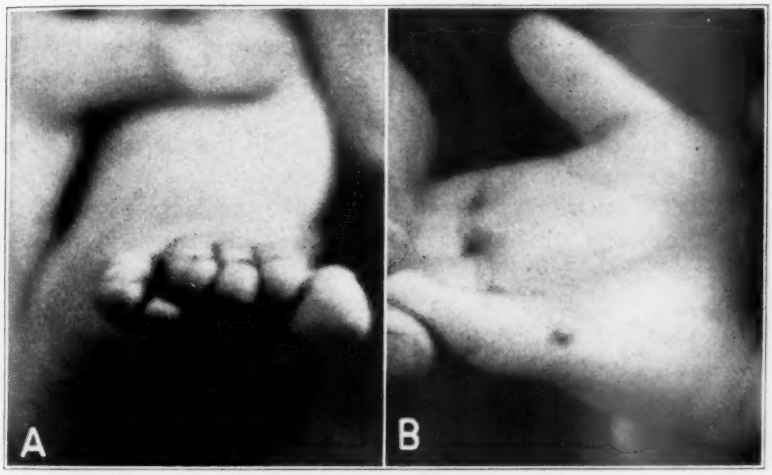


Fig. 5 (case 2).—*A* shows the supernumerary toe arising from the midportion of the medial aspect of the right little toe, and *B*, the rudimentary digit at the base of the right little finger, similar to that of the brother (fig. 3).

## COMMENT

The cases recorded here illustrate effectively the strong familial tendency in the Laurence-Moon-Biedl syndrome and also bring out again the fact that the disease affects the children of only one generation, whose parents and ancestors are not affected. It can also be reemphasized that while all the cardinal signs of the syndrome may not be present in one person they are likely to exist among several affected members of a family. Another hereditary tendency was exhibited in this family in the frequent twinning, a trait transmitted through the paternal side. No such tendency is known to have been observed previously in association with the Laurence-Moon-Biedl syndrome, and it may have been irrelevant in this case.

Of thirteen children, five were apparently affected, three of whom died. The boy described here shows all the classic signs with the exception of hypogenitalism, and at the initial examination mild genital hypoplasia was thought to be present. Pigmentary degeneration of the retina, with night blindness, obesity of the type associated with dystrophia adiposogenitalis and mental retardation were definitely present. The small fibrous nodule found at the base of the right little finger represented rudimentary polydactylism. In addition, the child had genu valgum, a condition observed in several of the reported cases. It is to be noted also that the boy had a persistently low basal metabolic rate, although there was no other evidence of hypothyroidism. Cholesteremia, found in cases of hypothyroidism, was not present in this case.

In the second case, obesity, polydactylism and mental retardation were present. Retinitis pigmentosa, a constant finding, had not made its appearance, but it should be remembered that this condition may not occur until the age of 5 years. Whether or not hypogenitalism was present was not determined.

The variability of polydactylism exhibited in this family is characteristic of this feature of the syndrome. One child had six toes and six fingers symmetrically. Another had six toes bilaterally, but six fingers unilaterally. Still another had a loosely attached supernumerary finger, removed easily at birth. Two children had small fibrous nodules identical in size, character and location, representing rudimentary fingers. One of these had, in addition, an incompletely duplicated toe.

## SUMMARY

The general clinical features of the Laurence-Moon-Biedl syndrome (obesity, retinitis pigmentosa, polydactylism, mental retardation and hypogenitalism) are briefly discussed, and a family is described in which five of thirteen children of one generation were affected. Two of these five children came under my observation; in the family history the remaining three gave strong evidence of involvement. One of the living children presented all the classic features of the syndrome, except that genital hypoplasia was questionable. In the second patient, retinitis pigmentosa, a constant finding in this condition, was absent, but in a child of 2 years its ultimate appearance is still possible.

NOTE.—Since this article was submitted for publication another paper dealing with the subject has appeared (Warkany, J.; Frauenberger, G. S., and Mitchell, A. G.: Heredofamilial Deviations: I. The Lawrence-Moon-Biedl Syndrome, AM. J. DIS. CHILD. **53:** 455 [Feb.] 1937). An analysis was made of one hundred and two cases of complete and incomplete forms of the syndrome reported in the literature. Only twenty-four cases were examples of the complete syndrome. Important

consideration was given in this analysis to the presence of associated abnormalities (nystagmus, strabismus, dwarfism, atrophy of the optic nerve without retinitis pigmentosa, deformities of the skull and congenital heart disease). When listed with the five cardinal symptoms as anomalies of equal importance, these additional abnormalities appeared with the following frequency: nystagmus, 31 per cent; strabismus, 20 per cent; dwarfism, 17 per cent; deformities of the skull, 8 per cent; atrophy of the optic nerve without retinitis pigmentosa, 4 per cent; deafness, 4 per cent, and congenital heart disease, 3 per cent. Fourteen of the twenty-four instances of the complete syndrome these authors considered to be "supercomplete," in that one or more of the additional anomalies was present. Because of the frequent occurrence of these other anomalies, the authors concluded that the designation as a syndrome of the five symptoms recorded in the literature is unjustified.

Dr. D. P. Hornbogen, of Marquette, Mich., made the ophthalmoscopic observations.

# Progress in Pediatrics

## DIETETIC TREATMENT OF ECZEMA IN INFANTS AND IN CHILDREN

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BERLIN, GERMANY

The treatment of constitutional eczema is one of the most important tasks of the pediatrician, for eczema occurs frequently in infants and in children, it can be very distressing and its treatment requires a special knowledge of child nutrition which only the pediatrician is supposed to possess. Moreover, eczema and its treatment are also of great interest to the clinician, for in eczema he has a chronic inflammatory process obviously connected with disturbances of the metabolism in general and with disturbances of the metabolism of the epidermis in particular. The eruptions exposed to view can be considered as test objects, the reaction of which to nutritional and circulatory changes, as well as to ectogenic irritations, can be studied without troublesome laboratory methods. This means a unique opportunity to investigate a fascinating problem of pathology by simple bedside observation.

The conditions which are usually designated as eczema are not by any means a unified group. They are of at least two types, for which the pathogenesis is different. There is no doubt about this, and there is also no doubt that one must try to classify the condition properly in every case; for since the pathogenesis is different, the treatment must also be different. It is a fact that the treatment which is effective for one type will be useless for the other, and vice versa.

One must distinguish between seborrheic eczema (recently called seborrheic dermatitis by Moro), on the one hand, and true eczema on the other. Seborrheic eczema is a primary disturbance of the protein and the fat metabolism in the skin, resulting in dyskeratosis with secondary inflammation. True eczema is a primary exudative inflammation with secondary dyskeratosis. One may also differentiate true eczema from neurodermatitis; the latter is characterized by the absence of exudation and by the formation of lichen-like nodules and plaques, with localization in the deeper layers of the corium. In treatment, though, it is not important to distinguish between neurodermatitis and chronic eczema because the treatment of the two conditions is the same.

The distinguishing features are subtle, and in many cases transitional cutaneous lesions occur. Therefore, many dermatologists say that a differential diagnosis is not possible in the case of infants and children.

But it must be possible, for the reasons just given, and I hold that it is possible, at least to the extent that one can say: This patient shows mainly the symptoms of seborrheic eczema or mainly the symptoms of true eczema, and, accordingly, his condition will probably yield to the treatment found useful for one or the other type.

Seborrheic eczema, or seborrheic dermatitis, is characterized by the eruption of plaques with more or less fatty scales, and these plaques resemble those of psoriasis. Therefore, one also has the designation psoriasoid. The plaques can become confluent to form larger patches. This occurs especially on the scalp, a thick fatty crust being formed. The cheeks may be unaffected, but as often as not there is a hyperemic, scaly infiltration—the so-called milk crust. The disease shows a preference for regions which are exposed to maceration, particularly the genitocrural region, and all places where cutaneous surfaces are in contact, e. g., cutaneous folds, articular creases, the armpits, the bend in the elbows, the folds of the neck in fat children and the folds at the beginning of the lobe of the ear. The scope of the fissures and areas of intertrigo depend on the extent of the disease. An important fact is that regions where there is a considerable secretion of cutaneous fat, such as the scrotum, the navel and the margins of the eyelids, are especially susceptible. Blepharitis is a pathognomonic symptom of seborrheic dermatosis. The younger the child, the more marked are the extended, intertrigo-like cutaneous changes; the older the child, the more dominant are the psoriasis-like eruptions. In young infants, therefore, the characteristic type is that which, when fully developed, is called erythroderma, or Leiner's disease, which is distinguished by extensive, often universal, scaliness and redness of the skin resembling general intertrigo. In persons of every age, though more frequently in older than in younger children, there are partial forms, restricted to the head or the cheeks.

It has been known for years that the addition of from 10 to 15 Gm. of protein powder (such as calcium caseinate or a similar preparation) not only facilitates normal development but almost always leads to a cure of the dermatosis within three or four weeks. This fact led to the conclusion that mother's milk is not an entirely adequate diet for children with eczema. Some substance necessary for normal composition of the skin and normal metabolism of the epidermis must either be absent from breast milk or present in an insufficient amount, and this substance must be contained in the protein of the diet. In other words, seborrheic eczema in young babies is due to a specific insufficiency of food, related to a low supply of protein.

However, experience has taught still another fact. With a minority of breast-fed infants, the addition of protein has little or no effect but there is a quick recovery when mixed feeding with cow's milk is pre-

scribed; by far the best results are obtained by using skimmed milk or buttermilk, that is, a substance not only rich in protein but low in fat. From this fact one concludes that breast milk is unsuitable for children suffering from seborrheic eczema not only because there is something lacking in it (which is contained in protein) but also because there is too much of some harmful substance in it. This substance is fat. Proof that the fat metabolism of the skin is involved is found in the fact that seborrheic changes occur mainly in regions where there are numerous sebaceous glands, e. g., the scalp, the margins of the eyelids and the genitalia.

So much for the conclusions derived from clinical observation. Briefly, it may be said that they have been confirmed by experiments on animals. Seborrheic eczema occurs regularly when there is a lack of vitamin $B_2$ in the diet. György spoke of a cutaneous factor in protein; breast milk contains a little of it and cow's milk more, and there is a considerable amount in liver, yeast, potatoes and kidneys. It is not found in other meat. The harmful effect of fat has been demonstrated.

A study of erythroderma and seborrheic eczema in young babies teaches that the diet must be rich in foods containing the cutaneous factor (György) and that it must have a relatively or absolutely low fat content. This principle holds, even for older babies and for children. In these groups, too, one finds cases in which seborrheic eczema is caused by lack of the cutaneous factor. The condition is not infrequently found in dystrophic infants. The dystrophic condition proves that the diet is inadequate. It also occurs in older children whose diet is not well balanced. I have seen a number of cases, mainly during the World War and the period of inflation, in older children who lived almost entirely on bread, potatoes, cabbage and only a little bit of milk. With the better diet in the hospital their skin cleared up in three or four weeks.

The administration of an adequate amount of the cutaneous factor and the avoidance of too much fat are not the only prerequisites for recovery. Several other conditions must be fulfilled.

In the first place, there must be no dyspeptic disorder and no other infection. Seborrheic eczema never heals as long as diarrhea or a febrile complication is present. During an infection there may be an exacerbation of the eczema, or it may clear up after the infection has been overcome.

Obviously, when there is diarrhea a large part of the cutaneous factor present in the food is destroyed or lost in the thin stools. Besides, there is a greater need for all kinds of vitamins during infection. This fact has been especially studied with respect to vitamin C. Many infants first acquire scorbutic symptoms during an infec-

tion, and it is a recognized empirical rule that the administration of vitamins must be increased during an infection, particularly if it lasts for a long time. This, of course, holds true also for the cutaneous factor related to seborrheic eczema.

In the second place, seborrheic eczema—even when infection and diarrhea are absent—never heals if the child does not gain weight. Hence the stubborn eczema which lasts many months in the dystrophic child, even when his diet has a low fat content and a high protein content. The condition disappears in a few weeks when one eliminates the dystrophy. Curing dystrophy is not difficult; in most cases it can be done by giving the baby plenty of calories and a large supply of carbohydrate. It is well known that the dystrophic child in order to gain requires from one and one-half to twice as many calories as a normal child of the same weight. Above all, the dystrophic child needs an abundant amount of carbohydrates, which is best given in the form of malt extract and flour. It is not known why a gain in weight and the administration of carbohydrate are necessary to clear up seborrheic eczema, but it is known that even in the normal organism the protein and the fat metabolism do not proceed normally without an adequate supply of carbohydrate. One can therefore assume that with seborrheic eczema every sort of general metabolic disturbance impairs the condition of the skin.

In the third place, seborrheic eczema never heals as long as there is a pyogenic infection of the eruptions. Dietary treatment is often, but not always, sufficient to overcome the cutaneous complications. In particular, it is not sufficient when there is a chronic purulent discharge from the nose or ear, with consequent recurring infection of the seborrheic cutaneous lesions. In this instance energetic local treatment is indispensable. I do not want to discuss the local treatment in detail, but I should like to emphasize that I have seen good results from injections of human blood, of vaccine and of protein bodies.

Now I come to the difficult problem of the treatment of older infants who suffer from seborrheic eczema but thrive normally otherwise, presenting no recognizable general nutritional disturbance, whose diet does not lack the cutaneous factor. Here, intolerance for fat is one of the chief factors. In several infants who were receiving from 10 to 20 Gm. of butter in addition to their usual diet, I saw recovery from the dermatosis when the butter was omitted and recurrence when the butter was given once more for the sake of experiment. Of course, the cutaneous condition does not appear and disappear within a few days after the diet is changed, but only after two or three weeks. Furthermore, I know of several children who suffered from seborrheic eczema whenever they took cod liver oil for a few weeks. Therefore, even in older children the disorder must be treated by a diet low in fat

and rich in foods containing the cutaneous factor previously mentioned. Plenty of yeast should be added, on the assumption that for reasons unknown the need of the cutaneous factor is abnormally great.

If this regimen does not help, what shall one do? Seborrheic eczema in adults is thought to be related to insufficiency of the generative glands. I have seen many older children with stubborn eczema who showed symptoms of a disturbed balance of the endocrine glands, in particular, excessive deposits of fat and retardation of puberty. All the children recovered spontaneously in the course of the years, after puberty at the latest. The idea of treatment with "sex hormones" presents itself. This has been tried with adults, and some observers have reported good results. I have not seen such results in children, but I have treated three patients with thyroid, with surprisingly good effect. The patients were older children (aged from 4 to 14 years) for whom dietetic treatment alone had been unsatisfactory. After one or two months of treatment with thyroid substance the skin was clear, but there were recurrences in two of the patients after from four to six months. When the condition recurred; it was cleared up by the same treatment.

True eczema, in contrast to seborrheic eczema, is a moist dermatosis. The oozing is caused by a peculiar condition of the skin which results in an abnormally strong hyperemic and exudative reaction to hematogenous and external stimuli. This condition was classed by Czerny as exudative diathesis, and Unna spoke of lymphophilia of the skin, meaning a condition in which the skin when irritated in any way reacts by increased hyperemia and increased exudation.

Exudation is the first distinguishing feature of this type of eczema; the second is a syndrome which I should like to call the angioneurotic-pruriginous syndrome. It forms the basis of the symptoms of eczema which lead to the assumption that hypersensitivity, or allergy, is one of the components—eosinophilia and, above all, marked and sometimes desperate itching.

In some cases the exudative component dominates the clinical picture. Then one has wet eczema or crusted eczema. The oozing surfaces easily suffer pyogenic infection, and thick suppurative crusts are formed; the result is so-called impetiginous eczema. With little exudation and more desquamation, one has squamous eczema. Further, there are forms in which the angioneurotic-pruriginous component stands out more and more. The most severe form is infiltrated eczema, that is, squamous eczema in which, as a consequence of persistent scratching, there is diffuse pachyderma from chronic inflammation and stasis of the lymphs.

The dietetic treatment of true eczema is entirely different from that of seborrheic eczema. A diet which will cure the latter will be of no value or may even be harmful for the former. Therefore, the differ-

ential diagnosis must be made carefully. Sometimes this is not easy, because seborrheic eczema may occur in children with lymphophilia of the skin, and then this type of eczema also can ooze and form crusts. The same condition can be caused by pyogenic infection of the seborrheic eczema. In such cases the itching may also be intense. The most reliable feature in the differential diagnosis is the localization of the eruptions. Seborrheic eczema shows a preference for (1) regions which are exposed to maceration, e. g., folds of the skin and articular creases, and (2) hirsute regions where there is increased secretion of cutaneous fat, e. g., the head and the margins of the eyelids. In true eczema the folds are unaffected. The external irritation which determines the localization of the eruptions is not maceration or decomposition of fat but persistent slight rubbing of clothes and bed sheets. Hence the eruption is located mainly on the outer region of the limbs. There is no intertrigo, the margins of the eyelids are spared and the scalp is not involved to a maximal degree. One should look, therefore, above all for intertrigo; one should also look for blepharitis and for fissures at the corner of the eye and at the beginning of the lobe of the ear. However, even if the condition is limited to the cheeks it can be seborrheic. The same thing is true even if it is moist. Several times I have been able to make a diagnosis of seborrheic eczema solely by the finding of unobtrusive intertrigo in a fold of skin. In these cases I have been able to cure the disease in a few weeks with a diet low in fat and containing plenty of buttermilk; every other kind of milk was strictly prohibited.

This leads to a remark about the frequent occurrence of eczema in older breast-fed infants. In at least half of such cases the disease is not true eczema but seborrheic eczema, as is proved by the finding of mild intertrigo. The eczema is caused by the low protein content and the high fat content of breast milk and can be cured or improved by mixed feeding, skimmed lactic acid milk or buttermilk and additional food of low fat content being used. In many cases better results will be obtained in this way than if the mothers are forbidden to eat eggs, milk and certain other foods on the assumption that the child is allergic to them.

Now, about the treatment of true eczema: First, the treatment has to be dietetic, for constitutional eczema is beyond doubt alimentary in origin. The disorder is surely related to the milk. This can always be demonstrated. Eczema in a baby who drinks a quart of milk per day will improve in a few days if the milk is reduced to a few ounces, and, on the other hand, an increased amount of milk will make the condition worse. The same holds true, though to a lesser degree, if sodium chloride is added to the vegetables.

Is eczema a tropho-allergic illness? I do not venture to discuss this question. I would put it like this: Can the cutaneous test give indi-

cations for treatment? Almost all infants who have eczema show a positive reaction to egg white and usually to a half-dozen or more other foods. But the infants are given only milk or cereals, and the reactions to the cutaneous tests with milk and cereal are usually negative or doubtful. Furthermore, if the babies are put on a milk-free diet —a diet, perhaps, of liver or other meat, vegetable fat and cereals other than those previously given—and if all foods which cause positive reactions to cutaneous tests are excluded, there is still no improvement. Thus, according to my experience, cutaneous tests are of little value in cases of eczema in children. Of course I do not doubt their value for other disease—and the only way left is to find out empirically what is good and what is bad.

First, one must know something about the treatment of the exudative component of true eczema. It must be borne in mind that the sensitivity to inflammatory irritations as well as the intensity of the inflammatory reaction depends to some degree on the water and the sodium chloride content of the tissues. Consequently, a pathologic retention of water and sodium chloride in the skin means a tendency to increased hyperemia and exudation. This has been known to pediatricians for a long time. When the Gerson dietetic treatment of tuberculosis of the skin was published, pediatricians were the first to maintain that the effect was mostly due to the low sodium chloride content of the diet, and this fact is now almost generally recognized. In the first years of life the tendency to increased retention of water and salt is normally more marked than it is later; in children with lymphophilia of the skin the tendency may reach a pathologic stage. For lymphophilic children even the amount of salt contained in milk is too great, especially if much carbohydrate is given at the same time, for carbohydrate favors the retention of salt and water.

If there is considerable exudation, a diet containing little milk and a small amount of carbohydrate is indicated. Only from 200 to 300 cc. of milk per day is given, with vegetables, fruits and small amounts of cereal. To increase the protein content, from 10 to 20 Gm. of cottage cheese, meat or calcium caseinate can be added. The dehydrating effect is certain. Consequently, the secondary pyogenic infection of the eczema is rapidly cured because the eczematous areas are dried up and bacteria do not thrive on dry soil. If there has been much oozing, or if infection has played a considerable rôle, as it does in impetiginous eczema, and if the child has previously received large quantities of milk —1 quart (946 cc.) or more, as was formerly common—the eczema can disappear entirely. But if the conditions do not apply, the eczema is only changed from a moist to a dry one; it is not cured. That is, the angioneurotic-pruriginous component of eczema is not affected by this treatment.

How can this angioneurotic-pruriginous component be fought? The replacement of milk by other animal protein is useless, as has already been indicated. Therefore, a diet entirely of vegetables has to be tried. Soy bean milk has been recommended by Hill and others and apparently is widely used. With this product and suitable additional food, infants can be well nourished, even for many months. As far as the effect on the eczema is concerned, I should like to summarize my experience as follows:

Soy bean milk is certainly better than cow's milk, and with it the condition is often improved or cured. But improvement is slow; one has to wait many months, and supplementary external treatment must be applied constantly. Soy beans from which the fat has been removed may be more effective, but I have no experimental evidence on this point.

Quicker and surer results are obtained by a diet consisting mainly of fruit and vegetables. This has been successfully used for many years by the so-called dietary reformers and nature healers in the treatment of pruriginous dermatosis of adults. That excellent physician, Bircher-Benner, of Zurich, Switzerland, was the first to use a diet of fruit juice and almond milk for infants. Then Rudolf Hess and Schiff recommended almond milk, with banana pudding, vegetables and potato pudding, fruit juice, some flour and zwieback. The effect on the eczema, especially on the itching, is indisputable in some cases. Nevertheless, I have often seen poor results. What is the cause? From my experience, I believe it is the fat in the almond milk. Many patients suffering from eczema have an intolerance to fat similar to that of patients with seborrheic eczema; even a teaspoonful of olive oil can sometimes cause a turn for the worse. Therefore, I used a fruit-vegetable-carbohydrate diet free from fat. For the first two days only fruit and rice are given; then cereals, bread, vegetables, salad, tomatoes and potatoes are added. No salt is given, of course. Besides, from 10 to 20 Gm. of vegetable protein is given. I am satisfied with the frequency and the rapidity of beneficial results. The quick subsidence of the itching is striking, and I have been astonished again and again at the rapid disappearance of the pachyderma of infiltrating eczema.

Naturally this restricted diet cannot be used for a long period because it does not contain enough protein. After marked signs of improvement, certain additions are made. First buttermilk or cottage cheese is added, then meat and later vegetable fat, and so on. Only one food is added at a time, at first only in small quantities, and observations are made for several days to see if the itching recurs.

It seems to be true that tolerance is improved with this basic diet lacking fat and animal protein. In a little while other foods can be

tolerated which have previously been visibly harmful. Gradually, a well rounded diet suited to the individual patient is attained, with which the skin remains clear. From time to time it is well to institute a period in which the diet is strictly controlled. Fortunately, as is well known, eczema in the majority of cases has a tendency to improve spontaneously and finally to disappear after the end of the third year, so that a more liberal diet can gradually be used.

The reason for the effectiveness of the vegetable diet is not known. At any rate, its use is followed by reduced hyperemia of the skin. By capillary methods it has been shown that the vessels are overfilled with blood if the diet is mainly animal matter. Transition to a vegetable diet causes a regression of this fulness. The same observation has been made concerning the Gerson diet for tuberculosis. Since eczema is characterized by hyperemia and exudation, it must be improved by anything which makes the skin more anemic. Therefore, the effect of a vegetable diet can be understood. But how does the vegetable diet produce this effect? This is the real problem and at the same time the very problem of how eczema originates and how it is cured. I believe that the circumstances are somewhat as follows:

Starting with a primary congenital specific abnormal disposition, metabolism in the epidermis proceeds abnormally. Thus a gradual pathologic change in the material structure of the epidermal tissues takes place, especially in the nerves which control the capillaries. These nerves become hypersensitive to every internal or external stimulus which affects them. This means that hypersensitivity, or an allergic condition, is brought about—in other words, a disposition to an increased inflammatory reaction to hematogenous stimuli of alimentary origin and to external irritations.

This explanation is obviously only a hypothesis at present, but it indicates the direction in which further studies on treatment should be carried out. That is, the aim should be to transform the pathologic structure of the epidermis to a normal structure by diet and thereby to normalize the hyperergic or allergic mode of reaction. Such studies are urgently necessary. The dietetic methods previously discussed are, indeed, more effective than the earlier ones, but they are by no means ideal. Even if a diet had been found which was 100 per cent effective, one could not be satisfied. For then the situation would be comparable to that of diabetes before the era of insulin. The "insulin" of eczema must be found, a substance which will cure the eczema and still give the patient wide freedom with respect to his diet.

I need not discuss neurodermatitis in detail. As far as treatment is concerned, it can be regarded as a type of eczema in which only the angioneurotic-pruriginous component is present, while the exudative

factor is entirely absent. As a matter of fact, in many cases of eczema the condition is gradually transformed into neurodermatitis when the cutaneous lymphophilia peculiar to infancy disappears in the course of the years. In view of these circumstances, the dietetic treatment of neurodermatitis is the same as that of dry eczema. It is effective against the universal and disseminated forms and less so or entirely ineffective against the inveterate circumscribed forms, especially when the disease is localized in the bends of the elbows and the popliteal spaces. But even in cases of these forms a diet rich in fat can sometimes cause a turn for the worse.

At this time I cannot discuss the external treatment in detail. I should like to say, however, that it is often indispensable, even when the diet is correct. If the diet is all right, external treatment is much more effective than it is otherwise. The most reliable remedies are coal tar and its derivatives, though the pure product is best. Coal tar is also the best means of relieving the itching; but why must it be so black and why must it smell so bad that most mothers detest it?

Further, roentgen treatment is useful for circumscribed residual foci, especially in cases of neurodermatitis of the bends of the elbow and the popliteal spaces.

Experiments with desensitization do not yet permit any conclusion. They should be extended, not only with regard to foods but with regard to cutaneous bacteria. It is possible that hypersensitivity to the latter is significant in a number of cases.

Finally, one must not forget that sudden intermissions and even recovery occur sometimes spontaneously and sometimes as a result of general treatment, notably change of climate. A couple of weeks at the sea shore or the mountains, without any special diet, is often helpful when all other measures have failed.

The dietetic treatment of eczema is only in its beginning. I hope that in the future it will become a matter of great interest and will be worked over systematically by pediatricians. I believe these developments will be worth while.

# News and Comment

## GENERAL

**International Congress of Pediatrics.**—The International Congress of Pediatrics will be held at Rome, Italy, from September 26 to September 30, and papers will treat the following subjects: (1) neuropsychic diseases in pediatrics from the clinical and the social point of view; (2) mineral and water metabolism in infancy and its repercussions on the problem of artificial feeding, and (3) the problem of tuberculosis of childhood with relation to (*a*) modern studies on ultraviruses, (*b*) the possibility of contagion through the child and (*c*) prophylaxis and treatment.

Special reductions in railroad fares have been obtained in Italy and the principal countries of Europe on this occasion.

Detailed information can be had by addressing the Secrétariat Général du Congrés, R. Clinica Pediatrica Policlinico, Rome.

**Examinations of the American Board of Pediatrics.**—The American Board of Pediatrics will hold fall examinations as follows: On Sunday, October 17, at Chicago, after the meeting of Region III of the American Academy of Pediatrics; on Sunday, November 7, at Los Angeles, after the meeting of Region IV of the American Academy of Pediatrics; on Sunday, November 14, at Boston, after the meeting of Region I of the American Academy of Pediatrics, and on Tuesday, November 30, at New Orleans, before the joint meeting of Region II of the American Academy of Pediatrics and the Southern Medical Association.

# Abstracts from Current Literature

## Anatomy and Physiology

THE MAMMARY GLAND IN THE NORMAL ADOLESCENT MALE. F. T. JUNG and A. L. SHAFTON, Proc. Soc. Exper. Biol. & Med. **33**:455 (Dec.) 1935.

In careful measurements of 169 boys from 12 to 17 years of age, it was found that enlargement of mammary tissue is probably an invariable accompaniment of adolescent changes in boys. It was noted in 73 per cent of the boys in the 14.25 year age group and in 100 per cent of those in the 15.75 and 17.5 year age groups.

HANSEN, Minneapolis.

EFFECT OF DEXTROSE ON GASTRIC SECRETION. H. UFLACKER, Monatschr. f. Kinderh. **66**:251 (Aug.) 1936.

Uflacker found that a proprietary preparation consisting almost entirely of dextrose depressed gastric secretion. He concludes that there is no justification for its use as a stimulant of the appetite.

GERSTLEY, Chicago.

## Biochemistry; Bacteriology, and Pathology

EFFECT OF MUCIN ON INFECTIONS BY BACTERIA. W. J. NUNGESTER, L. F. JOURDONAIS and A. A. WOLF, J. Infect. Dis. **59**:11 (July-Aug.) 1936.

When sterilized gastric mucin is used instead of a saline solution as a menstruum for suspending various bacteria, the host is placed at a marked disadvantage when the combination is injected and may succumb to what would otherwise be a sublethal infection. This effect has been noted when injections were made intraperitoneally, subcutaneously and intratracheally.

The mechanism of the action is not yet understood. Mucin does not interfere with phagocytosis but inhibits the bactericidal properties of phagocytic cells. It enables bacteria to survive in the body of the host for longer periods without diminution in numbers, or it may allow the organisms to multiply and so cause the death of the animal. The viscosity and cohesive properties of the mucin appear to be important indexes to the effectiveness of mucin on bacterial infections.

TOOMEY, Cleveland.

THE BACTERICIDAL AND BIOLOGICAL PROPERTIES OF PHENYL MERCURIC SUBNITRATE. K. T. SASANO and E. M. MEDLAR, J. Infect. Dis. **59**:35 (July-Aug.) 1936.

Sasano and Medlar found that phenylmercuric subnitrate does not interfere with antigenic properties or immunologic substances. They found this mercury preparation nontoxic, though with large doses they had local inflammatory responses.

TOOMEY, Cleveland.

RELATION OF THE HERPES ANTIVIRAL PROPERTY OF HUMAN BLOOD TO SEX, PREGNANCY AND MENSTRUATION. N. P. HUDSON, E. A. COOK and F. L. ADAIR, J. Infect. Dis. **59**:60 (July-Aug.) 1936.

Under the conditions of their investigation, Hudson, Cook and Adair were unable to distinguish between the sexes as to incidence of the herpeticidal antibody, nor could they derive significant experimental data to explain the frequent susceptibility of women to infection with the virus of herpes simplex when pregnant, menstruating or experiencing certain other physiologic fluctuations.

TOOMEY, Cleveland.

## Metabolism; Infant Feeding; Milk and Other Foods

MOTHERS' MILK AVAILABLE DAILY FROM CHILDREN'S WELFARE FEDERATION. Health News **13**:150 (Sept. 21) 1936.

The Mothers' Milk Bureau of the Children's Welfare Federation, 325 East 38th Street, New York, collects mother's milk. This is frozen in wafers and supplied to physicians in all parts of New York State for 30 cents per ounce.

AIKMAN, Rochester, N. Y.

BREAST FEEDING: THE PUBLIC HEALTH POINT OF VIEW. H. C. NIBLACK, Illinois M. J. **70**:259 (Sept.) 1936.

This article is a part of the round table discussion of the pediatric section of the Illinois Medical Society at the latter's annual meeting in Springfield, Ill., on May 19, 1936.

Niblack is interested in the infant welfare activities of the public health organizations of the city much as Dr. Grulee is in those of the private organizations. The public health organizations of Chicago are trying to create an interest in breast feeding and to get the infants born in the city on the breast. As regards the attending staff of the official public health organization of Chicago, its heads have especially undertaken to make an effort to build up a belief in breast feeding and are training the nurses how to teach the mother to keep the baby on the breast. They are teaching their nurses the best method of supplementing the baby's best efforts in developing and maintaining a supply of breast milk, namely, manual expression.

A year ago Niblack and his associates made a city-wide survey of breast feeding from the standpoint of the hospitals. A study of the data showed that contact had been made with 6,665 infants born in hospitals; of these, 56 per cent left the hospital wholly breast fed, 29 per cent fed a mixed diet and 15 per cent artificially fed. Contact was made with 2,650 infants who had been born at home; of these, at the time of call, 83 per cent were still wholly breast fed; 8 per cent were on a mixed diet, and 8.3 per cent were artificially fed. The infant welfare conferences, attended largely by colored mothers, show a registration of babies over 90 per cent of whom are breast fed. The higher the class of a neighborhood the fewer are the breast-fed babies. Over 80 per cent of the babies born at the Cook County Hospital went home breast fed.

ORVILLE BARBOUR, Peoria, Ill.

VOLUNTARY FOOD HABITS OF NORMAL CHILDREN. C. SWEET, J. A. M. A. **107**: 765 (Sept. 5) 1936.

Sweet discusses his experiences in private practice with the child who has a poor appetite. An observation period of three weeks, during which the child is permitted to choose his own variety and quantity of food, usually reveals the fact that he is eating a varied diet and often that he is taking more food than was thought. For practical purposes one vegetable is as good as another; meat is a valuable food for which fish is the only substitute; not every child needs a quart of milk a day, and a high fat content in food decreases appetite. Too many parents are engaged in a futile and painful struggle with their children to get them to take a complete diet. Doctors must instruct parents in the methods of carrying out the education of the child in the taking of foods as well as prescribe diets. Healthy children, if permitted, will voluntarily choose an adequate diet from a well stocked family table.

BONAR, Salt Lake City.

DIET IN RELATION TO PHYSICAL EFFICIENCY. G. E. FRIEND, Brit. M. J. **2**:276 (Aug. 8) 1936.

This is a general discussion of what is an adequate balanced diet. A special study of the diet in Christ's Hospital for Boys and of that of a certain number of

public school children is described. There is a discussion as to the incidence of disease and other matters that are likely dependent on diet, with a criticism of the diet in the institutions surveyed and a suggestion for a well rounded diet.

ROYSTER, University, Va.

RATIONALE OF FREE SCHOOL MEALS. E. H. M. MILLIGAN, Brit. M. J. **2**:278 (Aug. 8) 1936.

This is a survey of the diets available to a large number of school children and of the defects of the school children which are supposed to be dependent on the deficiencies in their diets. The elemental food deficiencies are discussed and suggestions made as to improvement, with special reference to the correction of the deficiencies by school action.

ROYSTER, University, Va.

WASTING IN INFANCY. R. C. JEWESBURY, Brit. M. J. **2**:321 (Aug. 15) 1936.

Jewesbury discusses this large subject and outlines the causes as follows:

1. Dietetic errors
   - (*a*) Unsuitability of food in quantity or quality or both
   - (*b*) Mismanagement in the manner of giving food to the child
   - (*c*) Inability of the child to take the food given
2. Infection
   - (*a*) Gastro-intestinal
   - (*b*) Parenteral
3. Environment
   Bad hygiene, including poor social conditions and lack of "mothercraft"
4. Constitutional causes
   - (*a*) Congenital disease
   - (*b*) Exudative or other diatheses
   - (*c*) Neuropathic defects
5. Birth injuries
6. Prematurity
7. Marasmus or infantile atrophy
   (Since marasmus per se does not appear to fall strictly under any of the foregoing headings the author classes it by itself for special consideration.)

ROYSTER, University, Va.

GLYCOGEN AND THE METABOLISM OF CARBOHYDRATE. F. G. YOUNG, Lancet **2**:237 (Aug. 1); 297 (Aug. 8) 1936.

Young reviews Claude Bernard's work and that of Pavy and Pflüger in some detail. Then he takes up the modern evidence concerning the secretion of sugar by the liver. As Claude Bernard stated, the constancy of the blood sugar level depends on an accurate mutual adjustment between the production of sugar by the liver and the absorption of sugar by the tissues. Modern research has shown that the mechanism controlling this mutual adjustment is an extremely complex one, associated with at least three hormones, insulin, epinephrine and a factor or factors from the anterior pituitary gland, and possibly involving, in a manner as yet little understood, the cooperation of nervous centers in the pons and hypothalamus.

As far as is known, protein can be easily converted to sugar in the body, but for some reason the formation of carbohydrate from fatty acids is a matter of some difficulty, the process apparently being accompanied by the formation of ketone bodies. It would seem reasonable to suppose, therefore, that the liver stimulates the conversion of fatty acids into sugar only when it is forced to do so by lack of sufficient alternative sources.

Young finally reviews the various theories regarding diabetes and states his own views.

LANGMANN, New York.

PERSISTENT ACIDOSIS IN AN INFANT: CAUSE NOT YET ASCERTAINED. R. LIGHTWOOD, N. F. MACLAGAN and J. G. WILLIAMS, Proc. Roy. Soc. Med. **29**:1431 (Sept.) 1936.

The case reported occurred in a child 14 months old. She did well until the age of 7 months. At 10 months she was seen by the authors for the first time and at that time showed fair nutrition, a good color, hypotonic muscles and a trace of albumin in the urine. A presumptive diagnosis of calcinosis infantum was made. Two weeks later she was admitted to the hospital looking ill. She was suffering from bronchitis and bilateral otitis media. Biochemical investigation revealed acidosis, evidenced by a diminished alkali reserve. There was no ketosis. She made a good recovery and was discharged at the end of three weeks. The results of chemical examinations of the blood and of the urine over a period of some months are given in the report.

WILLIAMSON, New Orleans.

TREATMENT OF HYPOTROPHY. M. MAILLET, Nourrisson **24**:274 (Sept.) 1936.

After devoting attention to the selection of a proper diet, emphasizing the importance of the known vitamins and the stimulating effect of exposure to the ultraviolet rays, Maillet discusses various specific treatments, namely, injections of extracts of such organs as the pancreas, thymus, liver and spleen, as well as administration of desiccated thyroid gland by mouth. In a particularly rebellious condition, a series of injections of one glandular extract is followed successively by a series of injections of each of the other glandular extracts until the whole gamut of the endocrine glands has been run. Protocols of several successes are displayed.

MCCLELLAND, Cleveland.

POWDERED LACTIC ACID MILK IN INFANT FEEDING. A. BOHN, Nourrisson **24**: 287 (Sept.) 1936.

Powdered whole milk artificially acidified with lactic acid and enhanced calorically with added cereal or carbohydrate or both was used. Excellent gains are reported to have been obtained in thirty-five infants, some of whom were hypotrophic or suffering from congenital debility.

MCCLELLAND, Cleveland.

INFANT FEEDING AFTER THE SIXTH MONTH. E. LESNÉ, Rev. méd.-sociale de l'enf. **5**:321 (Sept.-Oct.) 1936.

Lesné advises that vegetables, cereals and fruits should be added to the diet of a baby at 6 months of age (fruit juice having been added at 3 months); at from 10 to 12 months, one egg should be added every other day; at from 15 to 18 months, meat and butter. He gives a general discussion of the vitamins and of the development of the teeth, also of the hours and the routine of infant feeding.

BROWNE, Detroit.

PROTEIN CONTENT OF MOTHER'S MILK OBTAINED AT VARIOUS TIMES DURING THE NURSING PERIOD. A. BIEBER, Riv. di clin. pediat. **34**:712 (Aug.) 1936.

Samples of breast milk were expressed before nursing, after one third of the nursing period (five minutes), after two thirds of the nursing period (ten minutes) and after the whole nursing period (fifteen minutes). No appreciable variation in the protein of the milk was found in any of these periods.

HIGGINS, Boston.

STUDY ON THE METABOLISM AND THE IMPORTANCE OF IODINE IN THE CHILD: THE CONTENT OF IODINE IN THE BLOOD OF THE HEALTHY CHILD BETWEEN BIRTH AND NINE YEARS OF AGE. G. CONCAS, Riv. di clin. pediat. **34**:727 (Aug.) 1936.

The method of Fellenberg was used to determine the iodine in the blood. Iodine is always found in the blood, even from birth. Up to puberty girls have on the average less in the blood than boys. The iodine content shows oscillation, even as much as 50 per cent in a given subject. Iodine is found in greater quantity in plasma than in whole blood. The iodine content of mother's milk shows marked variations in different women. Tables are given showing the amounts of iodine contained in common vegetables, fish and milk of various animals.

HIGGINS, Boston.

ASCORBIC ACID AND GLUTATHIONE IN COW'S MILK IN MANCHURIA AND MONGOLIA. M. SUGIURA, J. Orient. Med. **25**:239 (Aug.) 1936.

Using the Birch modification of the colorimetric method originally devised by Tillmans and his co-workers, Sugiura found the cevitamic acid content of the Manchurian cow's milk to be 2.28 mg. per hundred cubic centimeters. The quantity of glutathione in the same sample of milk is approximately half of that of cevitamic acid. The values for both of these substances are higher during the winter months than in a warm season. The cevitamic acid in milk may be destroyed by heating but only to the extent of 60 per cent of the original quantity irrespective of the duration and degree of heating. Glutathione has a greater tendency to be destroyed at high temperature. On exposure to the atmosphere for thirty minutes, the cevitamic acid diminishes to the extent of 37 per cent, while no changes occur in the glutathione. The minimum daily dose of cevitamic acid preventive of scurvy in guinea-pigs is 0.556 mg. per two hundred grams of body weight.

KATO, Chicago.

ASCORBIC ACID CONTENT OF MANCHURIA PAPRIKA (SAPSICUM ANNUM L. VAR. GROSSUM SENDT). M. SUGIURA, J. Orient. Med. **25**:275 (Aug.) 1936.

By quantitative determinations of the cevitamic acid in Manchuria paprika, Sugiura arrived at the following conclusions:

1. There is a seasonal variation in the cevitamic acid content, the ripe pods being richer than the unripe.

2. The quantity diminishes with length of storage.

3. On mincing and exposing the pods to the atmosphere the acid is rapidly oxidized during the first twenty minutes and more slowly thereafter.

4. Capsaicin in paprika can be completely removed by a single treatment with ether for three minutes.

5. Approximately 6 per cent of the total cevitamic acid in the pepper is lost when the capsaicin is removed with ether.

6. When capsaicin is removed with permanganate, nearly 12 per cent of the acid is lost.

7. The iodine-reducing substances contained in the pepper are cevitamic acid and glutathione, both of which are present in the ripe pods, in the proportion of 1:1.7, whereas in the unripe ones glutathione is absent.

KATO, Chicago.

BASAL METABOLISM IN CHILDREN. KWIK TJIE TIOK, Maandschr. v. kindergeneesk. **5**:474 (Aug.) 1936.

In children with catarrhal jaundice the author usually found decreased basal metabolism. He made use of Krogh's respiration apparatus.

VAN CREVELD, Amsterdam, Netherlands.

## Vitamins; Avitaminoses

A Case of Carotenemia and Diabetes Mellitus with Necropsy Report and Analyses of Liver for Carotene, Vitamin A, Total Fat and Cholesterol. A. C. Pariente, C. H. Present and E. P. Ralli, Am. J. M. Sc. **192**:365 (Sept.) 1936.

The occurrence of a high level of carotene in the blood of diabetic patients has been reported. The average level of carotene in the blood of normal persons during fasting is 0.109 mg. per hundred cubic centimeters, and that in the blood of diabetic patients is 0.262 mg. The source of the increase in the blood carotene in diabetic persons is a matter of speculation. The case of a 45 year old white man with a history of diabetes mellitus of two years' duration is reported. Prior to the administration of carotene, the carotene in the blood of this patient was higher than normal. Following the administration of carotene, it rose to 0.540 mg., and at this level clinical evidence of carotenemia was observed. Postmortem examination revealed deposits of carotene in the mesenteric fat and in the arterial plaques.

Henske, Omaha.

Vitamin C Content of Sweat. T. Cornbleet and E. R. Pace, Arch. Dermat. & Syph. **34**:253 (Aug.) 1936.

Cornbleet and Pace report the content of cevitamic acid in human sweat as from 0.55 to 0.64 mg. per hundred cubic centimeters. This content is almost the same as Eckelen reports for blood serum, i. e., 0.50 mg. per hundred cubic centimeters of blood serum. The amount is about constant in normal persons and seems to be independent of the amount of sweat secreted in a given period. There seems to be no difference in the amount as between the white and the colored race; the amount is the same for the two sexes and is constant from adolescence through middle age.

Dulin, Iowa City.

The Comparative Antirachitic Efficiency of Vitamin D in Irradiated Milk, Metabolized (Yeast) Milk and Cod Liver Oil. R. M. Bethke and others, J. Nutrition **11**:21 (Jan.) 1936.

The results of previous studies by other workers do not all agree concerning the relative effectiveness of the different forms in which vitamin D may be supplied or of the different methods by which it may be derived, when tested by use in the prevention and treatment of rickets.

Bethke and his collaborators in the experiment reported attempted to obtain additional information on the subject. Working with chicks, they found that it required ten times as many rat units of vitamin D in metabolized milk as in irradiated milk to produce the same antirachitic effect. Other experiments have indicated that in the case of the rachitic infant equivalent amounts of vitamin D in metabolized milk and irradiated milk are equally efficacious. The authors deduce from these observations that the infant and the chick differ greatly in their response to these two forms of vitamin D in milk.

Equivalent numbers of rat units of vitamin D in cod liver oil and irradiated milk were equally efficient in preventing rickets among chickens.

Munns, Winnetka, Ill.

The Tissue Response to Subcutaneous Injection of Cod-Liver Oil. J. Davson, Lancet **2**:737 (Sept. 26) 1936.

Favorable results from the local application of cod liver oil to wounds and burns have been described by several investigators.

In Davson's experiments adult rabbits were used. Subcutaneous injection of fish liver oils produced marked stimulation of phagocytes, fibroblasts and young capillaries. Davson interprets this reaction as of a nature to facilitate healing.

Langmann, New York.

EXCRETION OF VITAMIN C IN THE URINE. P. ROHMER, N. BEZSSONOFF, R. SACREZ and E. STOERR, Compt. rend. Soc. de biol. **116**:1414 (July 11) 1934.

The violet reaction of Bezssonoff was used in determining the presence of vitamin C in the urine. In the rat and the bird the violet reaction occurs in the urine for many days after withdrawal of the vitamin from the diet. This probably means that these animals synthesize vitamin C.

However, the guinea-pig and the human infant during the first year of life act similarly with respect to vitamin C. The ability to excrete the vitamin is rather great during the first year, when the decrease in the amount becomes considerable. In the reaction a unit is considered to be the amount of violet intensity which is produced by 0.001 mg. of hydroquinone dissolved in 1 cc. of water or a solution of five-tenths-normal cevitamic acid. Infants were given cevitamic acid in their diets. The intensity of reaction varied in four infants (aged from 3 to 8 months) from 15 to 20 units for a period of three days. In two infants (aged 10 and 11 months) the intensity of reaction decreased from 12 to 7 units in three days. In four infants past 11 months of age, the intensity of reaction decreased from 17 to 0 units in twenty-four hours.

The phenomenon is not sustained in infants over 1 year of age.

WAHL, Cleveland.

RÔLE OF FAT-SOLUBLE VITAMINS IN THE SYNTHESIS OF VITAMIN C IN THE ANIMAL ORGANISM. P. ROHMER, N. BEZSSONOFF and E. STOERR, Compt. rend. Soc. de biol. **118**:56, 1935.

The feeding of polished rice alone to rats and birds has been shown to provide urine (free from vitamin C) negative by the Bezssonoff reaction in from four to five days. (The reaction of Bezssonoff may be explained as follows: 1 unit is the intensity of a violet color produced by 1 mg. of hydroquinone dissolved in 1 liter of water or by a solution of five-tenths vitamin C. The discoloration of urine is measured for vitamin C by the foregoing standard.)

The authors fed infants some dried milk, very poor in vitamin C. The Bezssonoff test was practically negative. Then, by adding yeast, which contains some vitamin C, this vitamin was excreted in the urine. On adding cod liver oil to the diet, the reaction became appreciably positive. The thought is that vitamin A is synthesized in the presence of vitamin C by bile and that, since carotene is present in green foods, the two are essential for a proper synthesis of vitamin C.

WAHL, Cleveland.

HYPERTROPHY OF THE SPLEEN IN EXPERIMENTAL RICKETS. G. MOURIQUAND, A. LEULIER and A. COEUR, Nourrisson **24**:265 (Sept.) 1936.

Rats on rachitogenic diets had relatively larger spleens than those on normal diets. This splenomegaly was not reduced when the animals were treated with viosterol. The largest spleens were found in rats placed on rachitogenic diets plus strontium carbonate, even though they also received viosterol.

MCCLELLAND, Cleveland.

VITAMINS A AND D IN TUNA OIL. G. BROGI, Clin. pediat. **18**:531 (Sept.) 1936.

Because tuna oil is available in the Italian fishing industry, Brogi studied its value as a substitute for cod liver oil. Albino rats fed a rachitogenic diet (McCollum diet no. 3143) showed a satisfactory response to both oral and parenteral administration of tuna oil. This oil had a prophylactic effect whether administered orally or parenterally, and a curative effect when given orally, to albino rats kept on a xerophthalmogenic diet (Frontali). It also seemed to have a trophic effect when given either orally or parenterally and had a favorable influence on erythropoiesis. The serum lipase (method of Michaelis) was elevated

after the oil was exhibited. The numbers of animals used in these experiments were quite small, not more than seven in any instance. The reproductions of the roentgenograms are not very clear.

DOOLEY, New York.

STUDIES ON THE VITAMIN C CONTENT OF ORANGE PEEL AND ITS PHARMACEUTICAL PREPARATIONS. H. C. HOU, Chinese M. J. **50**:1227 (Sept.) 1936.

At the Henry Lester Institute of Medical Research, Shanghai, Hou made determinations of the cevitamic acid in orange peel, using the chemical titration technic of Bessey and King. Chinese medicinal orange peel usually showed a moderate amount of vitamin C. The effect of drying was to reduce the vitamin C below that found in fresh orange. Hou determined the cevitamic acid in tinctures of orange peel and found it to be low. Extracts of orange peel made with 90 per cent alcohol were compared with watery solutions of cevitamic acid, the latter undergoing rapid destruction. The alcoholic extracts retained a fairly high amount of cevitamic acid for four days, but after two weeks there was little cevitamic acid found in the tinctures. He concludes that if a tincture of orange peel is to be used because of its cevitamic acid, the preparation should be fresh. More cevitamic acid is extracted from fresh orange peel by the process of infusion than by the tincture method. Cevitamic acid in extracts of orange peel is utilized well by guinea-pigs, but there is an incomplete absorption of the cevitamic acid in most vegetables.

NEFF, Kansas City, Mo.

## Hygiene; Growth and Nutrition; Public Health

SUBSTANCES PROMOTING NORMAL AND ABNORMAL GROWTH. J. NEEDHAM, Brit. M. J. **2**:701 (Oct. 10) 1936.

This is a general discussion of the subject of the paper, which does not lend itself to abstracting. It is a more or less discursive article on the general interaction and interdependence of various vitamins, with special stress being laid on the synthesism of vitamins A and D and their interdependence, and reference is made to a number of observations. The author feels that the presence of sulfur is necessary to the action of vitamin A and possibly also to that of vitamin D.

ROYSTER, University, Va.

CHILD HYGIENE IN HUNGARY. M. PENKERT, Gaz. d. hôp. **109**:1110 (Aug. 5) 1936.

Penkert calls attention to the economic difficulties in Hungary as a cause of the infant and child mortality, which is unfavorable when compared with that in Western Europe. Yet definite progress has been made, as shown by the fact that between the years 1920 and 1933 the rate dropped 32.6 per cent for the first year of life, 45.2 per cent for the second year, 65 per cent for the period between the second and sixth years and 55 per cent for that between the sixth and eleventh years.

The mediums through which knowledge of better care of children is propagated are:

1. The Hungarian Institute of Hygiene, founded in 1920, with the help of the Rockefeller Foundation. It is the hygienic adviser to the government, establishes model district health units, helps physicians through its staff of visiting nurses, supplies vaccines free, offers free use of its laboratories and in case of epidemics dispatches capable, specially trained physicians from its central organization.

2. Children's hospitals of the universities.

3. Asylums for Abandoned Children. This organization cares for the infants in its homes (hospitals) and afterward places them in supervised foster homes.

4. The "Stefania" National Association for the Protection of Mothers and

Infants. This association carries on the prenatal care of infants, maintains feeding clinics and supplies the needy ones with free milk.

5. The Hungarian League for the Protection of Children. This organization maintains convalescent homes, fresh air schools and special schools for tuberculous children.

Digestive disorders in infants during the summer months and tuberculosis in older children are chiefly responsible for the unfavorable statistics.

The children in the larger cities have periodical medical examinations in the schools. It is planned to extend this service to the rural districts.

KAJDI, Baltimore.

INFANT MORTALITY IN AUSTRIA. ERNST FÜRTH, Monatschr. f. Kinderh. **67**:1 (Sept.) 1936.

Fürth publishes a series of tables giving the death rate and birth rate as well as the number of deaths from congenital debility in each of the various provinces of Austria during the last ten years. The number of stillborn children is included in a special table. There is also a short table of infant mortality in Germany for the year 1932.

GERSTLEY, Chicago.

## Prematurity and Congenital Deformities

THE CHICAGO CITY-WIDE PLAN FOR THE CARE OF PREMATURE INFANTS. J. H. HESS, J. A. M. A. **107**:400 (Aug. 8) 1936.

The plan discussed has been in operation for a year. While the results of this year's organized effort to reduce the death rate of premature infants do not offer material for drawing conclusions in this respect, a drop in deaths of all infants born in this metropolitan area from 47.7 per thousand live births in 1934 to 40.1 in 1935 seems to be significant to the extent that this plan may have helped lower the death rate of all new-born infants. There was a definite decrease in the number of stillbirths. Of especial importance are antepartum care of the mother and avoidance of extreme narcosis during labor as well as of traumatism and chilling of the infant during resuscitation. Breast milk, intelligent nursing care and proper instruction of mothers in the care of the breasts and the baby tend to reduce mortality. Follow-up visits lower both mortality and morbidity.

BONAR, Salt Lake City.

CONGENITAL DEFORMITIES OF MECHANICAL ORIGIN. D. BROWNE, Proc. Roy. Soc. Med. **29**:1409 (Sept.) 1936.

Browne divides up the possible mechanical disasters that may befall the fetus into arbitrary categories and discusses them separately. The forces that may be applied, with their effects, are as follows:

1. Normal mechanical pressure on a fetus in the normal position.
   - (*a*) Bending of the back
   - (*b*) Calcaneus position of the feet
   - (*c*) Dimples over bony points in contact with the uterine wall.
2. Normal pressure and normal development of the fetus plus abnormal position
   - (*a*) Talipes equinovarus
   - (*b*) Malposition of toes
   - (*c*) Postural torticollis
   - (*d*) Displaced ears
   - (*e*) Facial paralysis
   - (*f*) Mutual deformity of the feet and face
   - (*g*) Acrocephalosyndactylia.

3. Normal mechanical and hydraulic pressure plus defective development, the defective development having, of course, nothing to do with mechanical influence of any kind

(*a*) Congenital dislocation of the hip
(*b*) Congenital fracture of the tibia
(*c*) Club hands

4. Normal hydraulic pressure and normal position with increased mechanical pressure. In this group there should be an increase in the severity of those three stigmas of pressure which the author described in the normal infant (1).

5. Normal hydraulic pressure plus increased mechanical pressure plus abnormal position

(*a*) Clubfeet of the usual type with degeneration of muscles and joints
(*b*) Atypical talipes with degeneration of muscles and joints
(*c*) A displaced finger showing arthrogryposis confined to that finger
(*d*) Spina bifida with talipes and degeneration of the muscles and joints of the legs
(*e*) A condition similar to (*d*), with mutual deformities of the head and feet
(*f*) A dimple over a displaced coccyx
(*g*) Talipes with dislocated hip and defective development

6. Pressure of amniotic bands

7. Spasmodic muscular pressure

(*a*) Formation of a sternomastoid tumor
(*b*) Dislocation of a normal hip
(*c*) Fracture of a tibia with backward angling
(*d*) Pressure sores on the sole of the foot
(*e*) Birth fractures

8. Increased hydraulic pressure. Photographs of most of the deformities outlined accompany the articles.

9. Deformities not due to mechanical causes

(*a*) Local failures of formation
(*b*) Ring constrictions of the extremities
(*c*) Sprengel's deformity
(*d*) Achondroplasia and various forms of dwarfism

10. In this paragraph the author gives alternative explanations of some of the conditions described, such as degeneration of muscle, dimples, talipes, congenital fracture of the tibia and arthrogryposis. In concluding he narrates some arguments against the mechanical causation of deformities.

WILLIAMSON, New Orleans.

THE QUESTION OF ACARDIA. B. SCHMID, Ztschr. f. Geburtsh. u. Gynäk. **113**: 172 (Sept. 25) 1936.

Schmid reports a case of acardia and reviews the literature on the subject. He discusses the genesis of this malformation and establishes its relationship to the teratoma.

ADAIR and POTTER, Chicago.

TYPE E: MULTIPLE ANOMALIES OF THE SKELETON, ENLARGEMENT OF THE LIVER AND SPLEEN AND MENTAL RETARDATION. C. DE LANGE and L. WOLTRING, Acta pædiat. **19**:71, 1936.

Two cases are described which are similar to those reported by Hurler under the title "Concerning a Type of Multiple Anomalies, Particularly of the Skeleton," representing a condition which Ellis, Sheldon and Capon have designated as

gargoylism. The distinguishing clinical features of gargoylism are chondro-osteodystrophy, corneal opacities, enlargement of the liver and spleen and mental deficiency. The disease is familial. It exhibits many points of resemblance to the familial syndrome of constitutional anomalies which has recently come to be known as Morquio's disease and to that described by Leri as familial pleonosteosis. The first case of gargoylism to be recorded in the United States was that described by Putnam and Pelkan (Am. J. Dis. Child. **29**:51 [Jan.] 1925).

The patients described by De Lange and Woltring were brothers. Both showed thick, short bones, stubby hands and fingers, hourglass-shaped nails and limitation of extension of the shoulder and knee joints together with marked enlargement of the liver and spleen. Both children were mentally retarded. One was of normal size; the other was a dwarf. In both patients the results of the galactose tolerance test suggested a disturbance of liver function. Neither patient exhibited the clouding of the corneas, the widening of the sella turcica and the serious mental deficiency which are characteristic of gargoylism. For this reason they are reported as illustrative of a special clinical subgroup, designated by the initial of the family name of the children as type E.

McCune, New York.

## New-Born

A Consideration of Some of the More Serious Conditions Encountered in the New-Born. A. H. Parmelee, Illinois M. J. **70**:250 (Sept.) 1936.

This article is timely and practical. It is too comprehensive to permit thorough abstracting. The original is worth reading in its entirety. Parmelee reminds one that more serious dangers threaten the human organism during the first days of its extra-uterine existence than in any other period of life. It is obvious that if one is to hope for a reduction in neonatal mortality a clearer understanding of the peculiarities of the physiologic functions and the pathologic changes in the new-born infant by all those who have to do with the care of the infant is essential. In his description of some of the more serious problems he discusses asphyxia, intracranial injuries at birth, atelectasis, hemorrhagic diseases of the new-born, infections, icterus gravis, fractures and prematurity.

Barbour, Peoria, Ill.

Delivery and Care of the New-Born Infant of the Diabetic Mother. L. M. Randall and E. H. Rynearson, J. A. M. A. **107**:919 (Sept. 19) 1936.

The mortality of the new-born of diabetic mothers is high in spite of the advanced knowledge of the treatment of diabetes. The occurrence of hypoglycemia in these infants was proved in the cases observed by Randall and Rynearson, and they consider it possible that some of the deaths of infants result from hypoglycemia. They have instituted a general plan to follow in managing the infant of a diabetic mother. The duration of the period of management depends on the degree of prematurity, the length of time before food and fluid can be taken by mouth and the duration of the period of readjustment of pancreatic function. Estimations of the sugar in the blood of the mother, the umbilical cord and the infant should be made immediately. After respiration has been established, the infant is placed in an incubator with a cover and the incubator is connected with an oxygen tank. For the first few hours from 40 to 50 per cent oxygen is given. Five cubic centimeters of 10 per cent dextrose solution is administered in each buttock, and the injection is repeated at intervals depending on the level of the blood sugar, the behavior of the infant and the latter's ability to take oral feedings. Ten cubic centimeters of a 10 per cent dextrose solution is given in four hours, and the injection is repeated every two hours for two days. Then 30 cc. of a lactic acid-karo mixture is given every three hours. If twitchings, convulsive movements or cyanosis appears, 10 per cent dextrose is given immediately, orally

or intramuscularly. The length of the period of danger from hypoglycemia cannot be predicted. This treatment is carried out until the infant can maintain itself normally. Seven cases are reported. Each of the infants was delivered by cesarean section.

BONAR, Salt Lake City.

THE DIAGNOSIS AND TREATMENT OF CYANOSIS OF THE NEWBORN. AARON CAPPER, M. Clin. North America **20**:99 (July) 1936.

The term asphyxia of the new-born is commonly employed to describe that condition in which spontaneous respiration is not established with sufficient promptness or force to maintain life. Any cause which may interfere with the placental circulation may produce some degree of asphyxia. The most common causes are: prolonged second stage of labor, the injudicious use of solution of posterior pituitary, maternal convulsions, narcotization, particularly from morphine or pentobarbital sodium, breech presentation, prolapsed cord or pressure on the cord and early separation or low implantation of the placenta.

While the pathologic changes in the blood of cyanotic infants are also present in asphyxia and while cyanosis is one of the signs of asphyxia, the former may occur as the result of a variety of other causes also, the most important of which are: (a) traumatic conditions of the infant, such as cerebral edema, cerebral hemorrhage or injury to the phrenic nerve, and (b) developmental anomalies of the infant, such as congenital heart disease, atelectasis of the lungs, enlargement of the thymus gland, diaphragmatic hernia, prematurity, micrognathy, infectious states of the infant, respiratory infections and sepsis and metabolic disturbances, especially tetany of the new-born.

Following this outline Capper discusses the modus operandi of the various causes of cyanosis, their differential diagnosis and methods of treatment based on the factors underlying the condition.

EUGENE SMITH, Ogden, Utah.

GONOCOCCAL ARTHRITIS IN THE MOTHER AND NEWBORN INFANT. JEAN M. MACLENNAN, Brit. M. J. **2**:121 (July 18) 1936.

MacLennan reports an unusual case of a mother infected with gonorrhea who gave birth to an infant who had ophthalmia in spite of the fact that mild protein silver drops were used promptly. The mother had multiple arthritis, and the infant had involvement of the metacarpal-phalangeal articulation of the left thumb, which ran a typical course of arthritis.

ROYSTER, University, Va.

BIRTH INJURIES OF THE CHILD. W. A. COCHRANE, Edinburgh M. J. **43**:137 (Sept.) 1936.

Cochrane, a surgeon at an Edinburgh hospital, discusses the mechanism, prognosis and early treatment of the common injuries sustained at birth.

The older theory of congenital torticollis, as offered by Stromeyer, was that the sternomastoid muscle was ruptured during delivery, causing a tumor, a hematoma, followed by organization of the hemorrhage; this theory has been replaced by the knowledge that fibrosis in the muscle can result only from venous obstruction. Brooks, of Chicago, showed experimentally that ligation of the vein alone will cause replacement of the muscle by a massive production of fibrous tissue. A sternomastoid tumor is not present at birth. It appears when the infant is from 10 to 14 days old. It is claimed that during labor temporary acute venous obstruction occurs in the muscle, this being due to occlusion of the thin-walled veins of the fetus when the head is put into a position of extreme rotation. Torticollis results probably from fibrosis of the sternomastoid muscle following the development and absorption of the so-called sternomastoid tumor of infancy.

Congenital wryneck must be treated. If it is mild it needs gentle manipulation and exercises; if these prove unsuccessful, manipulation is tried under anesthesia, and the correction is fixed with a plaster bandage for three weeks. Facial asymmetry is present in the late-treated patient, but in the patient treated early in life it diminishes and even disappears.

Birth palsy always has back of it a supraclavicular lesion of the brachial plexus and occurs usually in prolonged, difficult labor. The treatment in the newly born infant is the use of a light abduction splint, with the shoulder rotated outward, the forearm in supination and the wrist dorsiflexed. The application of a fairly large splint for a long period, massage and gentle stretching from the beginning are used to prevent contraction of the shoulder.

Injury at birth causes most cases of spastic paralysis. Cochrane states that it is surprising that the frequency of obstetrical lesions of the spinal cord has not interested more investigators and quotes the writings of Crothers, who reported observations on twenty-eight children with lesions due to traction during delivery at birth. Prevention of intracranial injury at birth is discussed.

NEFF, Kansas City, Mo.

RADIAL PARALYSIS DUE TO FRACTURE OF THE HUMERUS IN THE NEW-BORN. HARTEMANN and VIAL, Nourrisson **24**:295 (Sept.) 1936.

Paralysis of the radial nerve secondary to an obstetrical fracture of the humerus is rare. A case in which such complications were encountered is presented, and reference is made to a similar case described in the French literature. In the case reported, examination at the age of 4 weeks showed complete disappearance of the paralysis.

McCLELLAND, Cleveland.

KERNICTERUS (ORTH-SCHMORL) WITH AND WITHOUT ERYTHROBLASTOSIS IN NEW-BORN INFANTS. CORNELIA DE LANGE, Jahrb. f. Kinderh. **145**:273 (Nov.) 1935.

The clinical histories and pathologic observations in three cases of kernicterus are given. The literature is reviewed. The author feels that toxemia of pregnancy should be looked on as the most probable cause of hydrops foetalis, icterus gravis and congenital anemia in certain forms.

In most cases the destruction of blood in utero and during the first days after birth is accompanied by extramedullary formation of blood, which transcends physiologic limits. Erythroblastosis and erythroblastemia may or may not be present in a mild form.

With kernicterus, the yellow coloring is spread in a characteristic way over the brain, depending probably on differences in circulation to the cells. The most characteristic finding is the deep yellow of the inferior olivary nuclei. Deep yellow coloring and considerable necrosis are consistently found in the corpora subthalamica. Instructive colored plates are shown.

The author states that there are insufficient grounds for recommending splenectomy for familial icterus gravis.

LANDAU, Hannibal, Mo.

GENESIS OF PHYSIOLOGIC LEUKORRHEA IN THE NEW-BORN. LÓSZLÓ VON DOBSZAY, Jahrb. f. Kinderh. **145**:306 (Nov.) 1935.

Dobszy states that physiologic leukorrhea is dependent on the presence of follicular hormone, as is swelling of the breast gland in mastitis physiologica neonatorum. Leukorrhea with the characteristics of vulvovaginitis physiologica neonatorum (as he chooses to designate the condition) was produced experimentally in an older child by administration of follicular hormone.

LANDAU, Hannibal, Mo.

ASPIRATION OF AMNIOTIC FLUID AND ITS IMPORTANCE AS A CAUSE OF DEATH. W. BUFE, Ztschr. f. Geburtsh. u. Gynäk. **113**:265 (Sept. 25) 1936.

In a study of the lungs of 108 infants who were stillborn or who died within the first five days of life, evidence of aspiration of amniotic fluid was found in the lungs of all but 21. In 28 per cent the amount of amniotic fluid in the lungs was large; there were no concomitant pathologic conditions; hence the amniotic fluid present was considered the cause of death. Intra-uterine inspiration is caused by some interference with circulation through the umbilical cord. Pneumonia (eight cases) was present only when amniotic fluid had been inspired. The cause of the leukocytic infiltration is a qualitative abnormality of the amniotic fluid, possibly a change in the hydrogen ion concentration.

ADAIR and POTTER, Chicago.

THE CAUSE OF ICTERUS NEONATORUM. A. GREIL, Ztschr. f. Geburtsh. u. Gynäk. **113**:298 (Sept. 25) 1936.

The cause of physiologic icterus neonatorum and the importance of this condition as a constitutional indication of the qualitative and quantitative adequacy of the bone marrow, liver, spleen and capillary walls are discussed. Icterus gravis occurs when the germinal cells are of the best quality, and an unusually healthy mother produces a well developed, well nourished fetus. Such new-born infants have an abnormally large number of erythrocytes, and the physiologic destruction which takes place immediately after birth in order to bring the number of cells to the level necessary for extrauterine life is therefore of course excessive. This excessive destruction poisons these infants. The cells produced are quickly destroyed, and the excessive number may not be demonstrable clinically. Autopsy, however, discloses dysplasia of erythropoietic tissue.

ADAIR and POTTER, Chicago.

SEVEN CASES OF DERMATITIS EXFOLIATIVA NEONATORUM (RITTER). KAYO GI, J. Pediat. (Tokyo), no. 436, Sept. 20, 1936, p. 1320.

Gi reports his clinical observations on Ritter's disease. Four boys and three girls presented the disease during the first three weeks of postnatal life. In six patients, the initial lesions were vesicular, only one patient showing a diffuse erythematous rash at the onset. One infant, a girl, from whose lesions a positive culture of Staphylococcus aureus was obtained, died; all the others recovered. There was slight leukocytosis with a relative increase in eosinophils, the highest being 31 per cent. Serologic tests and urinalysis gave negative results. Local treatment with zinc in oil or in starch, together with internal administration of viosterol, produced a favorable outcome.

KATO, Chicago.

NECROSIS ADIPOSA NEONATORUM. K. BOJLÉN and S. PETRI, Acta pædiat. **19**:123, 1936.

The total number of cases of necrosis adiposa neonatorum which have been reported up to the present time is approximately one hundred. The disease has been described under a variety of terms: "induration curable cutanée du nouveau-né par traumatisme obstétrical" (Marfan), "sogenannte Sklerodermie der Neugeborenen" (Mayerhoffer), "circumscripte, symmetrische Fettsklerose im Säuglingsalter" (Keilmann), "sclerema neonatorum" (Gray), "traumatic necrosis of the subcutaneous fat of the newborn infant" (de Val and Bolin), "adiponecrosis subcutanea neonatorum" (Carol and van der Zande) and "adiposclerosis subcutanea neonatorum" (Nakagawa). The number of histologic examinations which have been recorded hardly exceeds twelve. Chemical and bacteriologic evidence relating to the etiology of the disease is scanty. As might be expected, numerous theories have been devised to explain the phenomenon; in these, emphasis is placed on obstetrical trauma and on the effect of chilling. As to pathogenesis, Unselm holds

that the essential feature is the splitting of neutral fats into their respective components. The fatty acids remain in the tissues either in the crystalline form or as calcium soaps. The subcutaneous fat of the newly born infant contains relatively large amounts of palmitic acid, a substance which has a higher melting point than either oleic or stearic acids and which also combines readily with calcium. However tempting the theories, none has yet been proved.

Two cases of necrosis adiposa neonatorum have already been reported from Queen Louise's Hospital for Children, in Copenhagen; a third case is presented from the same institution. The patient was an infant who was born asphyxiated; transitory fever and convulsions led to repeated intramuscular injection of whole blood obtained from her father. When the infant was 14 days old, ligneous infiltration of the subcutaneous tissues was detected in the region of the buttocks and thighs; the overlying skin exhibited a reddish violet hue; its temperature was not increased. The process continued to advance for about two weeks and by then had involved most of the back. Two weeks after the onset, as the last of the new lesions developed, the earliest ones commenced to resolve. The infant was entirely well in less than four months after the onset of illness. Histologic examination of a piece of tissue removed from the affected area showed extensive necrosis of the subcutaneous fat together with foreign body and reparative reactions. The histologic features were closely comparable with those recorded by previous observers.

Emphasis is placed on the benign prognosis for necrosis adiposa neonatorum and on the present complete ignorance concerning its etiology. The paper includes a tabular recapitulation of the cases previously reported in the Scandinavian literature, and a comprehensive bibliography is appended.

McCune, New York.

Dextropositio Cordis in Relation to Pneumothorax and Pulmonary Atelectasis in New-Born Infants. N. I. Heybroek, Maandschr. v. kindergeneesk. **5**:443 (Aug.) 1936.

Heybroek could observe in three new-born infants that the heart was transposed to the right side, with the result that roentgen examination was made. In this way an exact diagnosis was possible. In the first case the finding was atelectasis of the right lung; in the second spontaneous pneumothorax on the left side, and in the third, enormous hypertrophy of the right ventricle with complications. He recommends roentgen examination of any new-born infant in whom dextropositio cordis is present and advises caution in making the diagnosis of atelectasis.

van Creveld, Amsterdam, Netherlands.

Tuberculosis in a New-Born Infant. E. Gorter, Nederl. tijdschr. v. geneesk. **80**:3710 (Aug. 15) 1936.

In this clinical lecture a case of probable placental tuberculous infection is described. The disease started when the baby was at the age of from 2 to 3 weeks, with abdominal symptoms, which seemed to point to the sepsis caused by an infection of the umbilical cord. The baby died at the age of 36 days. The autopsy demonstrated the presence of general tuberculous infection. The parents were both suffering from open tuberculosis.

van Creveld, Amsterdam, Netherlands.

## Acute Contagious Diseases

Milkborne Scarlet Fever and Sore Throat Outbreak. Health News **13**:121 (Aug. 3) 1936.

In sixteen cases of scarlet fever, nine in adults and seven in children, the disease was traced to a single supply of grade A raw milk. Hemolytic streptococci were isolated from four persons living on the farm and the same organisms were detected in the milk from one cow.

Aikman, Rochester, N. Y.

RELATIONS OF ACID BASE EQUILIBRIUM TO THE PATHOGENESIS AND TREATMENT OF WHOOPING COUGH. JOSEPH C. REGAN and ALEXANDER TOLSTOOUHOV, New York State J. Med. **36**:1075 (Aug. 1) 1936.

Whooping cough produces profound and characteristic biochemical changes in the blood and tissues. The hydrogen ion concentration of the blood is increased; the inorganic phosphorus content is moderately or markedly diminished, while the carbon dioxide-combining power is within the normal range. In addition, there are a low normal (or subnormal) sugar content and an increased uric acid content of the blood.

The authors found that the administration of alkalis has a rapidly curative effect on whooping cough and may even abort the disease in early cases.

AIKMAN, Rochester, N. Y.

LATE RESULTS IN SIXTY-THREE CASES OF POLIOMYELITIS TREATED IN THE RESPIRATOR. M. BERNARD BRAHDY, New York State J. Med. **36**:1147 (Aug. 15) 1936.

Sixteen hundred and thirty-two patients with poliomyelitis were admitted to the Willard Parker Hospital in New York from January 1931 to December 1933. Sixty-three of these, about 4 per cent, received treatment in the respirator. Twelve with bulbar lesions were thus treated in 1931; all died during treatment. Patients with spinal conditions associated with paralysis of the intercostal muscles or of the diaphragm numbered fifty-one; of these, twenty-four, or 47 per cent, died during treatment. A follow up of the remaining twenty-seven patients was made after four and one-half years; thirteen of the twenty-seven patients died from nineteen days to two and one-half years after treatment. Of the fourteen who are still alive, only seven are up and about, and only two of these have no residual paralysis. Special attention is called to the frequent occurrence of massive atelectasis in patients with severe poliomyelitis.

AIKMAN, Rochester, N. Y.

OUTBREAK OF COWPOX, CAUSED BY A VACCINATION INVOLVING TWO FAMILIES AND TWO HERDS OF CATTLE. STANLEY W. SAYER and FRANKLYN B. AMOS, New York State J. Med. **36**:1163 (Aug. 15) 1936.

A milker who had recently been successfully vaccinated against smallpox infected animals of two dairies with cowpox. Practically all the cows were infected. These cows were the source of infection in eight cases of cowpox in human beings. None of these persons had been previously vaccinated, except one, who had been vaccinated thirty-eight years previously. Recently vaccinated persons in the infective stage of cowpox should not be permitted to care for dairy animals.

AIKMAN, Rochester, N. Y.

CURRENT PREVALENCE OF COMMUNICABLE DISEASES. Pub. Health Rep. **51**:1327 (Sept. 25) 1936.

In the period from Aug. 9 to Sept. 5, 1936, the incidence of poliomyelitis still continued above normal in the east south central region. The total number of cases reported for the country in this period was 626. For comparison, in the same period of 1935 there were 3,625 cases reported. The incidence of meningitis, scarlet fever, measles, influenza and typhoid fever continued low. The incidence of typhoid was the lowest in this period that it had been in the last eight years. The number of cases of smallpox continued high, the disease being still confined to the north central, mountain and pacific regions. The mortality from all causes was 10.1 per thousand, which is slightly higher than at any other period during the past three years.

SANFORD, Chicago.

THE HAEMOLYTIC STREPTOCOCCUS, WITH SPECIAL REFERENCE TO SCARLET FEVER. D. BREWER, Brit. M. J. **2**:620 (Sept. 26) 1936.

This is the third article in the symposium. Brewer considers the streptococcus public enemy no. 1 in Europe. He considers it the commonest of all causes of temporary inconveniences and also of permanent defections from normal health. The infections are divided into two groups: (1) the three notifiable diseases, scarlet fever, erysipelas and puerperal fever and (2) a miscellaneous group embracing almost every form of sickness from which man suffers. All of them are similar fundamentally. He considers the reservoir of the streptococcus to be the human nasopharynx. With reference to interaction of scarlet fever and the puerperium, he has the following impressions: 1. Parturient women are just as likely to suffer from scarlet fever as are nonparturient women. 2. If the implantation is at the normal site—the throat or nose—both diseases run their normal course. 3. If the implantation is in the genital tract, the result is serious. He feels that the most frequent infection of streptococcic origin in wounds is scarlet fever, but that it is the least serious. He also indicates that a generation ago the infection of scarlet fever was probably more fatal than it is now—that it has become attenuated. He thinks that scarlet fever is recurrent—that it is only the rash phenomenon which is not recurrent. He thinks that streptococcic tonsilitis is in many instances identical with scarlet fever but that there is evidence in many cases of definite immunity; the subsequence is that he does not think scarlet fever is a specific disease. In discussing the possible connection between scarlet fever and acute rheumatism, he thinks that rheumatism is badly named. He thinks it is rarely acute and rarely rheumatism and that the etiologic factors cannot be separated from those of scarlet fever. The two illnesses are biologically manifestations of the same process. Considering erysipelas, he thinks this disease has changed little for many, many years but that its fatality has been increasing in the last few years. He thinks that the incidence of puerperal fever has increased during the past forty years, but that its fatality has declined. Of other forms of streptococcic lesions he has little to say, merely mentioning that they probably occur. Immunization and treatment are next discussed. As for methods of immunization, he is skeptical as regards most stages of the streptococcic infection. He feels that some success has been met in the prevention of scarlet fever. He thinks there is promise of an antistreptococcus serum in acute rheumatism, especially carditis, but he is not dogmatic. Immunization is not promised.

ROYSTER, University, Va.

ALLERGIC REACTIONS TO THE SCHICK TEST. H. J. PARISH, Lancet **2**:310 (Aug. 8) 1936.

Parish gives a brief summary of seven instances collected from the literature and seven additional instances on which he had notes. In most cases symptoms appeared within a few minutes after the Schick test was made. A wheal at the site of injection was the common local reaction. Puffiness of the face, scarlatiniform and erythematous rashes, faintness, cyanosis, dyspnea, bronchial asthma and other signs and symptoms were recorded.

LANGMANN, New York.

INTRAVENOUS OR INTRAPERITONEAL ANTITOXIN TREATMENT COMBINED WITH SHORT ISOLATION PERIOD IN SCARLET FEVER. H. S. BANKS, Lancet **2**:559 (Sept. 5) 1936.

This report is based on a study of a series of 1,877 patients treated intravenously with serum and 1,419 controls and a second series of 551 patients treated intravenously and 540 patients treated intraperitoneally with serum.

A single dose of from 10 to 20 cc. of scarlatinal antitoxin injected intravenously or intraperitoneally within the first three days after the onset was found

to modify considerably the course of simple and of septic scarlet fever. A substantial and significant reduction of morbidity was effected. The incidence of otitis media was reduced to one-third, and that of nephritis to less than one-seventh, of the incidence in untreated controls.

The intraperitoneal treatment yielded results almost identical with those of intravenous treatment.

LANGMANN, New York.

SOME OBSERVATIONS ON THE RELATION BETWEEN CLINICAL TYPES OF DIPHTHERIA AND CULTURAL TYPES OF CORYNEBACTERIUM DIPHTHERIAE. P. M. ANDERSON, N. E. GOLDSWORTHY and H. K. WARD, M. J. Australia **2**:350 (Sept. 12) 1936.

The authors studied 184 patients with diphtheria in respect to the relation of the clinical type of the disease to the cultural type of the organism. Eighty-eight patients were infected with the mitis type of Corynebacterium diphtheriae, and seven of these died, giving a mortality of 7.9 per cent. Ninety-six patients were infected with the gravis type and twenty-five of these died, giving a mortality of 26 per cent. Malignant and submalignant diphtheria were much more frequent in the gravis type of infection and accounted for the high mortality.

GONCE, Madison, Wis.

PROPHYLAXIS, TREATMENT AND BACTERIOLOGY OF PERTUSSIS. A. D. GARDNER, Proc. Roy. Soc. Med. **29**:1273 (Aug.) 1936.

Gardner's interest in whooping cough dates from a visit to Denmark many years ago, when he saw the bacteriologic-diagnostic service in full operation, and from a subsequent epidemic in his own family, when neither he nor his physician could say which of the children had been attacked. The impotence of the medical practitioner in clinical diagnosis is due to the late and inconstant appearance of the sole characteristic symptom, the whoop. Gardner agrees with certain American writers who suggested the abandonment of the name whooping cough and the substitution of the old term pertussis, which would wean physicians and the public from their age-long diagnostic reliance on the unreliable whoop. This was confirmed in an epidemic occurring in a school where only one fifth of the pupils whooped and few even had recognizably spasmodic coughs. Bacteriologic progress has been based on the acceptance of Bordet's discovery of a small hemophilic bacillus known as Haemophilus pertussis as the cause of the disease. This is still questioned by a few writers, who pin their faith to a virus. The evidence for and against the bacillus as the sole etiologic agent is briefly reviewed. The author then shows that the points put forth that pertussis is caused by a virus are not convincing. He sums up by saying that pertussis is "an infection of the respiratory tract with H. pertussis, generally giving rise to a spasmodic cough."

The evidence on which a diagnosis can be based may be divided into clinical, hematologic and bacteriologic. Clinical diagnosis in the early stages is impossible. The hematologic evidence is based on a lymphocyte count and the complement fixation test. The bacteriologic test would become much simplified and more popular if a substitute could be found for fresh blood. The intradermal test has been tried by a number of workers and is thought to be worthless by some. The use of vaccines in whooping cough is discussed fully. In summing up the vaccine treatment Gardner says that the position of prophylactic vaccination is substantially better than it was a few years ago. This measure is effective both in reducing the chances of attack and in attenuating the disease in those attacked. In regard to treatment he states that he does not propose to discuss the difficult subject of specific therapy. The best hope is to anticipate or accelerate by suitable injections the immunity otherwise acquired only in the attack, and with the new

powers of control afforded by the bacteriologic discoveries of the last ten years one may hope to see a substantial improvement as soon as the country as a whole becomes, in transatlantic phraseology, sufficiently "whooping cough conscious."

WILLIAMSON, New Orleans.

INTESTINAL DIPHTHERIA. ADAMASTOR BARBOZA, J. de pediat., Rio de Janeiro **3**:347 (Aug.) 1936.

A 6 year old child presented a high fever, abdominal distention and gas. All tests were negative. Barboza observed that the child had a very red throat with cervical adenitis. This led him to make cultures from the nose for diphtheria bacilli, which he found. Cultures of the stool showed the organism. After receiving 10,000 units of antidiphtheria serum the child recovered promptly. The author feels justified in reporting this case as an authentic case of intestinal diphtheria, as the cultures showed distinctive organisms.

SANFORD, Chicago.

ACUTE ANTERIOR POLIOMYELITIS IN BASEL AND IN THE BASEL CHILDREN'S CLINIC. HELMUT GOLDBLUM, Inaug. Dissert., Basel, 1935.

The characteristic pathologic picture presented by the fifty-six children with acute anterior poliomyelitis admitted to the children's hospital in Basel during the years from 1918 to 1933 are described and discussed. Attention is drawn particularly to the symptoms indicating involvement of the vegetative nervous system and to the residual psychic reactions of nervousness and instability.

CRANE, Chicago.

TWO CASES OF MEASLES WITH CEREBRAL COMPLICATIONS. HERMANN ZISCHINSKY, Jahrb. f. Kinderh. **144**:353, 1935.

Two cases of measles with cerebral complications are reported. The first patient, a girl of 3½ years, had measles, followed in three weeks by symptoms suggesting encephalitis. This was followed in several weeks by streptococcic meningitis, which terminated fatally. The possible relation between these cerebral complications is discussed. No definite conclusions regarding the relationship were reached.

Another case, that of an 8 year old girl who acquired cerebral complications on the third day of measles, is reported. This child recovered fully.

The cerebrospinal fluid in the first case showed an elevated pressure during the period of encephalitis. The findings at the time of the streptococcic meningitis were characteristic for that condition. The spinal fluid of the second child was normal, except for slightly elevated pressure.

LANDAU, Hannibal, Mo.

THE NUMBER OF INCISIONS AND THEIR INFLUENCE ON SMALLPOX VACCINATION. MARTIN HOHLFELD, Jahrb. f. Kinderh. **145**:194 (Oct.) 1935.

The history of the technic of vaccination against smallpox is given, and the reason for the large number of scars formerly made is discussed. The conclusion is reached that the number of scars has no real influence on the subject's immunity. The percentage of successful vaccinations with but two incisions if these are made by one whose technic is good may far surpass that with four incisions made by another.

LANDAU, Hannibal, Mo.

THE ACTION OF HOMOLOGOUS AND HETEROLOGOUS SERUMS IN DIPHTHERIA. H BAAR, Klin. Wchnschr. **11**:1545 (Sept. 10) 1932.

An attempt was made to determine whether antitoxic serum of the same species would act more favorably in animals with diphtheria than heterologous serum. Rabbits were given repeated doses of diphtheria toxin, and their serum

was then used in the treatment of a series of rabbits given injections of diphtheria toxin. The results thus obtained were compared with those in a similar series of rabbits given horse serum of the same antitoxic content. For the treatment of the latter series, diphtheria antitoxin was diluted with normal horse serum to bring it down to the same titer as the rabbit antitoxic serum. The conclusion was reached that in rabbits the homologous serum was effective at a later period after the injections of toxin than the horse serum was.

Diphtheria toxin was injected intracutaneously in human subjects and the effects of human serum of known diphtheria antitoxic content were compared with those of ordinary diphtheria antitoxin of the same titer. The evidence suggested that the human serum was superior when used against the effect of the toxin in the human skin. Baar suggests that definite conclusions cannot be drawn from these experiments because of the complexity of the problem.

SILVERMAN, Syracuse, N. Y.

TREATMENT OF MALIGNANT DIPHTHERIA WITH BLOOD TRANSFUSIONS. H. BENEDICT, Klin. Wchnschr. **11**:1549 (Sept. 10) 1932.

Benedict administered transfusions of from 400 to 500 cc. of blood along with small doses of diphtheria antitoxin to patients with malignant diphtheria. He states that he employed this treatment in nine children with the most severe malignant pharyngeal diphtheria, in all of whom recovery seemed improbable, but seven recovered completely. What diphtheritic paralysis ensued developed late and disappeared in a short time. No cardiac complications developed in any of these children. He attributes the results to a combination of effects, in which the antibody content of transfused blood has to be considered in addition to the influence of the volume of fluid on the heart and blood vessels.

SILVERMAN, Syracuse, N. Y.

SEROLOGIC DIAGNOSIS OF DYSENTERY IN NURSLINGS AND SMALL CHILDREN. GYULA TAMASI and ZOLTAN TEVELI, Monatschr. f. Kinderh. **64**:363, 1936.

The agglutinins in the blood serum were studied in 138 cases of dysentery. Tests were made against the Shiga-Kruse bacillus and against the Flexner groups A, B, D and H. It was found that persons with dysentery had agglutinins against most of these types. The amount of agglutinin against a specific type of infection was usually increased over the amount of other agglutinins found. To be of value in diagnosis in observing the agglutinin reaction one must take into consideration all the agglutinins against dysentery found in the patient's serum and their relation to one another.

GERSTLEY, Chicago.

RECURRENCES IN POLIOMYELITIS. FRIEDRICH WILDTGRUBE, Monatschr. f. Kinderh. **66**:265 (Aug.) 1936.

A case of poliomyelitis is reported in which on the forty-first day a second attack occurred involving muscles which had been spared by the first attack. Three days later there seemed to be another recurrence. In the diagnosis of a condition with such an unusual course one must distinguish between cases with true recurrences and cases in which ganglion cells had been injured during the first attack and were temporarily exhausted. True recurrence may be fatal, so even in mild poliomyelitis one should not declare the patient out of danger until after six weeks.

GERSTLEY, Chicago.

EFFECT OF SIMPLE SERUM ON THE SCHICK REACTION. WOLFGANG KIEHL, Monatschr. f. Kinderh. **66**:339 (Aug.) 1936.

Ever since diphtheria antitoxin was introduced there has been an undercurrent of opinion that its success cannot be attributed entirely to the antitoxin content.

With the advent of the Schick test there are new possibilities of reopening the subject. Kiehl gave children with a positive Schick reaction injections of serum from both horses and cattle, containing less than 0.005 unit of antitoxin. No effect was observed. He next used a serum containing 0.01 unit or less. This serum caused disappearance of the positive Schick reaction. He then used commercial antitoxin twenty times the amount that was in the serum just mentioned. No effect was observed. The conclusion is obvious that there are factors other than antitoxin in therapeutic serums which affect their success.

GERSTLEY, Chicago.

BLOOD GROUPING IN SCARLET FEVER. LISELOTTE BERNECKER, Monatschr. f. Kinderh. **66**:391 (Aug.) 1936.

In five hundred cases of scarlet fever the blood grouping was studied. It was found that no particular blood group was in preponderance. As far as could be made out clinically, an exudative-lymphatic constitution was of greater significance as a predisposing cause.

GERSTLEY, Chicago.

PATHOGENICITY OF DIPHTHERIA BACILLI FOUND IN DIPHTHERIA CARRIERS. ALINE AICHAM, Monatschr. f. Kinderh. **67**:39 (Sept.) 1936.

Strains of diphtheria bacilli taken from the noses and throats of patients sick with diphtheria and patients recovered from diphtheria frequently lost their pathogenicity after a certain length of time. This fact has been known but it has perhaps been overemphasized. While certain organisms may become avirulent, in some cases after a period of time avirulent organisms may become virulent again. Aicham believes that one must not underestimate the danger to the community of the carrier.

GERSTLEY, Chicago.

CLINICAL OBSERVATIONS ON POSTVACCINAL ENCEPHALITIS. Y. IWASAKI, J. Pediat. (Tokyo), no. 436, Sept. 20, 1936, p. 1229.

Iwasaki reports three cases of postvaccinal encephalitis. These occurred in infants from twelve to fourteen days after vaccination. The infants were 2 years, 13 months and 7 months old, respectively. The oldest infant died of complicating bronchopneumonia after a temporary recovery from the encephalitis; in the second, optic atrophy developed, resulting in bilateral blindness; the third recovered completely without complications. Eight cases of postvaccinal encephalitis reported in Japanese literature and 74 instances collected from foreign literature are analyzed in detail in tabular form. From the analysis the author deduces the following conclusions: 1. The incidence of the disease is most frequent during the first year of life (34.9 per cent), gradually falling after the second year and being seldom seen after the eighth year. 2. Both sexes are equally affected, the males slightly predominant (54 per cent). 3. The disease develops most commonly after a successful initial vaccination, the incubation period being from seven to fourteen days. 4. In approximately 60 per cent of the cases the condition terminates in complete recovery, but death may follow complications, particularly bronchopneumonia. 5. The prognosis is bad in young infants, improving with the age of the infants. 6. The duration of the disease is from one week to one month or more. 7. The chief complications of the disease are: cerebral atrophy, disturbance of speech, spasticity of limbs, facial paralysis, blindness, ptosis of the eyelids and paralysis of shoulder muscles. 8. The clinical manifestations of the disease are: fever, choreiform movement, opisthotonos, lockjaw, loss of or increase in knee jerks, facial paralysis, Babinski's sign, tremor of the finger-tips, headache, Kernig's sign, paralysis of the ocular muscles, convulsions, paralysis of the limbs, vomiting, stiffness of the neck, stupor, clouding of the sensorium and excessive perspiration.

KATO, Chicago.

## Acute Infectious Diseases

RAT-BITE FEVER. T. J. MARSHALL, Arch. Pediat. **53**:664 (Oct.) 1936.

Marshall reports three cases of what appeared to be rat-bite fever. Spirochaeta morsus-muris was recovered in one case. In two of the cases the diagnosis was made from the history and the results of physical examination. Two patients were successfully treated with stovarsol, administered by mouth.

ORR, Buffalo.

THE SPREAD OF TULAREMIA THROUGH WATER AS A NEW FACTOR IN ITS EPIDEMIOLOGY. S. P. KARPOFF and M. I. ANTONOFF, J. Bact. **32**:243 (Sept.) 1936.

Karpoff and Antonoff studied an epidemic of tularemia occurring in Russia and came to the following conclusions after a careful review of their data: In the outbreak in question the tonsils, the mouth, the mucosa and the conjunctiva formed the portals of entrance of infection. The anginal form predominated, and the typhoid form came next while a number of patients showed the glandular-ocular form. A new mode of spread of tularemia was proved experimentally and bacteriologically, i. e., the spread by water. The quantity of micro-organisms in the infected water courses may sometimes be so considerable that isolation of the infective agent does not meet with great difficulties. The cultures that were isolated from water did not differ in regard to virulence from those that were isolated from suppurating lymph glands of the patients. When these cultures were tested on guinea-pigs, death followed in 100 per cent of the inoculated animals, and the organs showed the changes characteristic of tularemic infection.

STOESSER, Minneapolis.

SCREW WORM INFESTATION. W. R. WALLACE, J. South Carolina M. A. **32**:213 (Sept.) 1936.

This disease has been greatly on the increase in animals, and now is affecting human beings. Any one who has an open lesion, such as impetigo, which is common in children, is prone to become affected. A case in a farmer 72 years of age is reported. The treatment consists in irrigations with boric acid and application of benzene compresses.

WESTON JR., Columbia, S. C.

TYPHUS FEVER. L. C. SHECUT, J. South Carolina M. A. **32**:215 (Sept.) 1936.

A review of the literature on Brill's disease is given. Four cases are reported, in two of which the Weil-Felix test was positive, while in two it was negative. The patients had the same symptoms and made uneventful recoveries.

WESTON JR., Columbia, S. C.

MALARIA IN CHILDREN. W. PIERRE ROBERT, South. M. J. **29**:738 (July) 1936.

The problem of control of malaria is far from solved. During the past few years the morbidity and mortality have increased.

Congenital malaria definitely exists in hyperendemic areas, and the infection is maintained principally by the child population. This is explained by the fact that young children acquire immunity slowly.

There is no safe and effective sterilizer, but plasmochin will prove valuable if the dose can be standardized for infants.

Characteristics distinguishing childhood malaria from malaria in adults are: (1) the frequent absence of fever, (2) its irregularity, if present, (3) the predominance of digestive symptoms, (4) the common excitation into activity of latent conditions and (5) the relatively large doses of quinine necessary for cure.

While leukopenia is the rule, many children with malaria have a high leukocyte count, with a high percentage of polymorphonuclear neutrophils.

Quinine in large doses is the safest drug to use for children. It is seldom necessary to use the intravenous route.

In treating malaria the general condition of the patient must be kept in mind.

Pyelitis is a frequent complication in malarial patients and must be differentiated from the true malarial condition.

SCHLUTZ, Chicago.

RHEUMATIC FEVER AND RHEUMATIC HEART DISEASE IN WEST VIRGINIA. W. C. STEWART, West Virginia M. J. **32**:420 (Sept.) 1936.

Each year rheumatic fever is causing the death of many children and leaving countless others maimed and crippled. The acute rheumatic phase of the disease is much milder in the more temperate climates and is often overlooked. There is urgent need of more careful study and better understanding of rheumatic fever and rheumatic heart disease. Recurrence is the rule. Heredity is a feature. A typical case is reported. Focal infections and other associated conditions are discussed.

SHAWKEY, Charleston, W. Va.

AETIOLOGICAL RELATION OF THE STREPTOCOCCUS HAEMOLYTICUS TO THE "RHEUMATIC" DISEASES. W. GOLDIE and G. J. GRIFFITHS, Brit. M. J. **2**:755 (Oct. 17) 1936.

Goldie and Griffiths discuss the relationship between Streptococcus haemolyticus and rheumatism with special reference to the possibility of a previously existent streptococcic infection leading to sensitization before rheumatism sets in.

ROYSTER, University, Va.

OBSERVATIONS ON THE MECHANISM OF RHEUMATIC FEVER. A. F. COBURN, Lancet **2**:1025 (Oct. 31) 1936.

Three phases are recognized in an attack of rheumatic fever: (1) an acute infection of the upper respiratory tract (lasting a few days); (2) a period of complete absence of clinical symptoms and signs (from a few days to six weeks—generally one to two weeks); (3) a period of rheumatic manifestations.

A small minority of patients acquire rheumatic fever after pharyngitis caused by the hemolytic streptococcus.

The response of two antibodies which can be estimated most accurately has been studied particularly, viz., antistreptolysin and precipitins to the M substance of the infecting agent.

Wilson and others have shown that the titers of antistreptolysin in children under 3 years of age are low and do not rise following infections with the hemolytic streptococcus.

A rheumatic subject who contracts a series of hemolytic streptococcus infections acquires acute rheumatism only when infection is followed by a rise in the titer of antistreptolysin. The initial rise corresponds quite closely to the onset of symptoms. However, in no case did the titer reach its maximum at the same time as the symptoms and the sedimentation rate, but it continued to rise even after the latter had begun to subside.

The data presented here in conjunction with certain findings referred to seem to indicate that the immune responses of the rheumatic patient differ from the normal person's in that they are delayed. There may also be a delay in the final elimination of hemolytic products from the body.

LANGMANN, New York.

OBSERVATIONS ON CONGENITAL MALARIA. M. MACCIOTTA, Clin. pediat. **18**:632 (Oct.) 1936.

Macciotta tabulates the data on the carefully studied cases of fifteen malarial women who were delivered of uninfected babies in the obstetrics clinic of the

University of Modena. A sixteenth malarial woman had a thin anemic baby, who died with fever and convulsions on the ninth day of life. Permission for an autopsy was not obtained. The mother's blood showed parasites, and about 80 per cent of the red cells in the placental blood contained parasites, but none were seen in the blood of the cord or in the infant's blood. A seventeenth malarial woman, who had contracted the disease three months before parturition, had a baby who died on the third day of life. There were parasites in both the cord and the infantile blood, but the organs showed no gross evidence of the disease at necropsy. The placenta showed neither gross nor microscopic damage, but there were parasites in about 70 per cent of the placental red cells. The eighteenth patient had twins who died on the eleventh and twelfth days of life, respectively. Parasites were found in the maternal and placental blood, and in the cord and peripheral blood of both infants at birth. Macciotta comments on the rarity of placental transmission in consideration of the large number of gravid women with malaria and reviews the various theories to be found in the literature relating to such transmission.

DOOLEY, New York.

EPIDEMIOLOGICAL, BACTERIOLOGIC AND CLINICAL PECULIARITIES OF A HOSPITAL EPIDEMIC OF BRESLAU ENTERITIS. LUDWIG SEITZ, Jahrb. f. Kinderh. **145**:31 (July) 1935.

Seitz points out that the pediatric literature is incomplete regarding the problem of Bacillus paratyphosus, especially in regard to the Breslau type of enteritis. The Breslau organism is considered to be within the paratyphoid B group. Formerly there was much controversy.

The described epidemic occurred in a hospital. The epidemic was typical neither of spread by contact nor of spread by food.

Of the forty-four patients studied bacteriologically, forty-three had typical symptoms of enteritis. Only two showed a varying course, one of whom had a mixed infection (another organism in addition to the Breslau organism); the other child had an invasion of the blood stream.

Recurrences were infrequent and on the average lighter than the primary illness. The mortality was about 11 per cent.

Postmortem observations were not especially characteristic. Catharrhal inflammation of the bowel and parenchymatous degeneration of the organism were noted.

Antibodies were usually demonstrable. The optimal time for finding antibodies is between the second and the fourth week.

LANDAU, Hannibal, Mo.

FATTY DEGENERATION CAUSED BY EXCESS OF CHOLESTEROL ESTERS IN ACUTE YELLOW ATROPHY OF THE LIVER CAUSED BY TYPHOID FEVER: REPORT OF A CASE. H. BEUMER, Jahrb. f. Kinderh. **145**:265 (Nov.) 1935.

An 8 year old, previously healthy child became suddenly ill with high fever and diarrhea. This attack was followed later by icterus, swelling of the liver, coma and death. Typhoid bacilli were found in the stools. The Widal reaction was positive in a titer no higher than 1:25.

At postmortem examination the liver and spleen showed an extraordinary accumulation of cholesterol, probably of endogenous origin.

LANDAU, Hannibal, Mo.

EPIDEMIC MYALGIA IN CHILDHOOD. G. LINDBERG, Acta pædiat. **19**:1, 1936.

Epidemic myalgia—better known to American physicians as epidemic diaphragmatic pleurodynia or Devil's grip—was first described in 1856 by Jon Finsen, who witnessed an outbreak of the disease in Iceland. The earliest American report was published by Dabney in 1888. Epidemic myalgia has since been recognized in many countries, more frequently in Norway than elsewhere. The affinity of

the disease for children was noted by Homann in 1873. The present paper describes eighty cases observed in children during an epidemic which took place in Norrköping, Sweden, in the autumn of 1934.

Resembling previous outbreaks in the time of year at which it appeared, the epidemic arose and declined between mid-August and the end of October, i. e., within a period of two and a half months; the high point was reached about a month after the onset. Since the disease is not reportable, the total number of cases in each age group was not determined. Of the eighty children the largest number were between 7 and 12 years of age, although a good many were under 6 years. The clinical features of the disease were strikingly uniform. The onset was fulminating, without prodromal warning. Pain was the most characteristic symptom. It was usually intense and of a sticking or stabbing character but was not accompanied by local tenderness. It was referred to the chest in thirty-five cases, to the abdomen in thirty-one cases and to the epigastrium in sixteen cases; nine patients complained of accompanying pain in the arms or legs. The abdominal discomfort led frequently to an erroneous diagnosis of appendicitis. One patient who complained of pain in the neck also exhibited a palpable localized tumefaction of the sternocleidomastoid muscle. Next to pain, fever of a variable degree was the commonest manifestation. As in previous epidemics, exacerbations or recrudescences were the rule; these usually occurred after a day or two of apparent improvement and consisted of renewed distress and rise in temperature. The duration of the illness was variable but averaged a little over a week. Grippal symptoms were conspicuously absent, although slight reddening of the throat was present in twenty cases. In some instances the number of leukocytes in the blood was diminished; in others it was moderately increased. The sedimentation rate of the erythrocytes was usually somewhat accelerated. Friction rub or roentgen evidence of dry pleurisy, features which have been reported by some observers, were noted only five times; in no case did pneumonia or pericarditis occur. None of the patients presented digestive symptoms, and none had orchitis, although these features have characterized certain epidemics. Manifestations referable to the central nervous system are not common in epidemics of myalgia. However, in five cases of this series sterile, benign meningitis developed; this was characterized by subjective symptoms of meningeal irritation and by slight increase in the cell count and protein concentration in the cerebrospinal fluid. One patient had meningismus without changes in the spinal fluid.

There is little question but that epidemic myalgia is an acute specific infection of unknown etiology, which is presumably transmitted by personal contact. The period of incubation is probably between two and four days. The mechanism by which pain is produced is not understood; the essential pathologic features are myositis and serositis.

McCune, New York.

An Investigation of the Incidence of Intestinal Worms, Particularly of Trichuris Trichiura, in Patients of the Copenhagen University Children's Clinic. H. Roth, Acta pædiat. **19**:104, 1936.

Employing the Telemann-Schroeder concentration technic, which is generally used in the Danish hospitals, Roth searched the stools of 302 native infants and children for the ova of intestinal parasites. With few exceptions only one examination was made for each patient. Ova of Trichuris trichiura were found in the stools of 28 per cent of the patients; ova of Enterobius vermicularis in 3 per cent and ova of Ascaris lumbricoides in 3 per cent. In many cases the infestation with Trichuris was heavy. The figure relating to the incidence of Enterobius vermicularis was thought to be too low, since it was based on examination of feces and not on anal scrapings. The largest number of Trichuris-containing stools came from children suffering from diseases of the central nervous system. However, in only three cases was there reason to suspect that infestation with

Trichuris was productive of clinically demonstrable disease. Acetarsone was used therapeutically in a few cases of trichocephaliasis, but, although a large number of macerated worms were excreted, the infestation was not determined.

Roth compares his findings with those of other investigators in Denmark and elsewhere. He discusses the possible routes through which infestation occurs in Danish children. Surprise is expressed at the low incidence of Ascaris lumbricoides among the patients of the series studied. The bibliography is useful.

McCune, New York.

A Case of High Eosinophilia. B. E. J. Becking, Maandschr. v. kindergeneesk. **6**:17 (Oct.) 1936.

A boy of 2½ years, who had already discharged 2 ascarids and who had high fever and a palpable tumor in the flank, appeared to have 54 per cent eosinophilic leukocytes. No worm eggs were found in the feces. There was a sudden fall of the temperature to normal, with sudden disappearance of the tumor. Repeated examinations of the blood showed from 57.5 to 62.5 per cent eosinophils. After treatment with santonin and mild mercurous chloride 14 ascarids were passed. Later eggs of Trichocephalus dispar were always found. Gradually the eosinophilia diminished to normal values.

van Creveld, Amsterdam, Netherlands.

## Chronic Infectious Diseases

First Infection Type of Tuberculosis in Young Adult Life. J. A. Myers, Am. Rev. Tuberc. **34**:317 (Sept.) 1936.

The evolution of the first infection type of tuberculosis in the animal body probably proceeds as follows: Polymorphonuclear leukocytes ingest tubercle bacilli in the blood stream and, together with uningested bacilli, focalize in the small alveolar capillaries. About these focal accumulations large numbers of exudative mononuclears accumulate, which in turn grow phagocytic, ingesting both bacilli and polymorphonuclear leukocytes, and become the epitheloid cells of the tubercle. This focalization and walling-off before sensitization appears may be an important factor in making primary tuberculosis benign. Following the introduction of tubercle bacilli into the organism the tissues become sensitive to tuberculoprotein, a sensitivity manifest by a positive skin reaction in from three to seven weeks after infection. Following sensitization, if reinfection from endogenous or exogenous sources occurs, tuberculosis of the usually benign first infection type may be stimulated to activity and disease of the destructive type develop. Thus, while the nonsensitized child may tolerate comparatively heavy doses of tubercle bacilli and may present no outward manifestations of the infection, nevertheless within him a sensitivity develops which carries with it the likelihood of the development of destructive lesions should reinfection occur.

Eugene Smith, Ogden, Utah.

The Use of the B C G Vaccine Against Tuberculosis in Children. C. Kereszturi and W. H. Park, Am. Rev. Tuberc. **34**:437 (Oct.) 1936.

Eight years of carefully controlled study in the laboratory and the clinic have convinced the authors of the harmlessness of the B C G vaccine. Large amounts of living B C G organisms were injected into from 400 to 500 laboratory animals. All animals except one remained free from tuberculosis, and in the one instance accidental infection could not be excluded. Clinically, the vaccine was administered to 175 infants who were not known to have been exposed to tuberculosis, with the possible development of clinical tuberculosis in but one of them. Of 515 children vaccinated with living B C G organisms and exposed to tuberculosis, only 5 contracted the disease. From these patients organisms of the human, not the bovine, type were recovered. In 27 cases, the virulence of the B C G strain,

recovered from cold abscesses caused by the vaccination, could not be shown to have been enhanced by living in the human body for periods of from one to ten months.

The parenteral administration of the vaccine seems to be more effective than the oral since the tuberculosis death rate decreased to half when the oral method was used and to a fourth when B C G was injected intracutaneously or subcutaneously. Since this procedure is harmless and increases considerably the resistance to tuberculosis, its use should be urged as a public health measure in those who have not yet become infected and who may later become exposed to tuberculosis in their own families.

EUGENE SMITH, Ogden, Utah.

MAPHARSEN IN MASS TREATMENT OF SYPHILIS IN A CLINIC FOR VENEREAL DISEASES. O. M. GRUHZIT and R. S. DIXON, Arch. Dermat. & Syph. **34:** 432 (Sept.) 1936.

Gruhzit and Dixon report the use of mapharsen in the venereal disease clinic of a large city over a period of almost three years; 75,589 injections were administered to 4,841 patients. This drug when used in conjunction with a heavy metal was found to be prompt in action. It caused prompt and sustained reversal of a positive reaction of the blood. There were no severe unfavorable reactions, and no hemorrhagic encephalitis, hemolytic anemia, jaundice, severe exfoliative dermatitis or severe nutritional crises occurred. The mild reactions were fewer than those produced by arsphenamine. The advantages of mapharsen are that it is the active spirocheticidal agent and is not changed to a more toxic form within the body. It is eliminated rapidly, and there is no cumulative effect. The solutions are easily made and relatively stable. Exposure to air for several hours or agitation causes no change in their chemical nature or in their toxicity. The authors used 0.01 Gm. to 2 cc. of sterile distilled water. A dose of from 8 to 12 cc. can be administered rather rapidly—in from ten to twenty seconds. The drug does not produce local pain in the vein, thrombosis or sclerosis. Only two cases of disturbance of this type occurred. This seems to be a special advantage in the treatment of children with small veins. Perivascular injection or extravasation results in severe local pain, swelling and induration, which clears up in from three to five days without ulceration.

DULIN, Iowa City.

CONGENITAL SYPHILIS. R. C. MADDOX, Arch. Pediat. **53:**692 (Oct.) 1936.

The author presents his routine of treatment for congenital syphilis.

ORR, Buffalo.

MORTALITY IN TUBERCULIN-POSITIVE INFANTS. MIRIAM BRAILEY, Bull. Johns Hopkins Hosp. **59:**1 (July) 1936.

One hundred and seventy children, of whom seventy-two were white and ninety-eight Negro, found to be infected with tuberculosis before reaching 2 years of age have been kept under observation for periods ranging from one to five years. The total five year mortality for white children was found to be 13 per cent and that for the Negro children 31 per cent. Approximately 70 per cent of the deaths which occurred in five years of observation fell within the first year, mostly within the first six months following the discovery of infection. Of those admitted with involvement of the parenchyma of the lung, 31 per cent were dead within the first year of observation, no difference being observed between the two races in mortality. Among those whose initial roentgenograms showed no parenchymal involvement, mortality during the first year subsequent to the discovery of infection was 6.8 per cent. No deaths occurred among the forty-nine white children of this group, but there were seven deaths among fifty-four Negro children. In both white and Negro children, mortality has been more than twice as high in those known to be infected during the first six months of life, as in those whose

infection was discovered between the ages of 6 months and 2 years. In about 78 per cent of the white and 64 per cent of the Negro children of this study there was intrafamilial contact with a person whose sputum had contained tubercle bacilli. The children of each race with known exposure showed a slightly higher mortality than children not known to have been exposed.

AUTHOR'S SUMMARY.

RECOVERY OF VIRULENT TUBERCLE BACILLI FROM THE TISSUES OF SWINE INTENDED FOR FOOD. W. H. FELDMAN, J. Infect. Dis. **59**:43 (July-Aug.) 1936.

Attempts were made to isolate and type tubercle bacilli that were present in dressed carcasses of swine which had been retained on postmortem inspection for tuberculosis. Material was obtained only from carcasses in which the lesions of tuberculosis were slight or localized and which were "passed for food" after the diseased tissues had been removed. The left precural lymph node from each of 88 carcasses and the right internal iliac lymph node from each of 13 carcasses were obtained and cultures prepared. With a total of 101 specimens, tubercle bacilli were obtained from 4. Studies of pathogenicity revealed that all of the strains belonged to Mycobacterium tuberculosis avium.

This study should emphasize anew the importance of the problem of avian tuberculosis and should indicate that virulent tubercle bacilli may still be present in the carcasses of hogs even though all visible lesions of tuberculosis have been removed.

TOOMEY, Cleveland.

TUBERCULOSIS IN INFANCY AND CHILDHOOD. J. W. S. BLACKLOCK, Brit. M. J. **3**:324 (Aug. 15) 1936.

This disease is discussed rather widely under several headings:

*General Incidence.*—There is a total of 3,000 necropsies, the incidence of which is subdivided by ages. It is evident from this that the incidence of tuberculosis is exceptionally low in the first three months of life but thereafter gradually rises to a peak in the third year, after which there is a slight fall. The incidence is higher among girls than among boys.

*Immunity from Childhood Infection.*—The author feels that a latent minimal infection of childhood which has become quiescent probably gives rise to immunity of some degree and prevents tuberculous infection of an acute type. Such immunity, if it occurs, can be broken down by ill health or by massive or continuous infection by tubercle bacilli of either exogenous or endogenous origin.

*Primary Respiratory Tuberculosis.*—A consideration of the pathway of infection is helpful so far as prevention is concerned. There are five possible routes of infection. Three—the skin, eyes and genital organs—are of little importance. The main routes are the respiratory and the alimentary system. The former was the route in 65.2 per cent of the cases studied. The lesion at the portal of entry into the lung is characteristic, consisting of a localized patch of caseous bronchopneumonia, which in most instances is about the size of a pea. This can occur only in nonallergic persons; it occurs most frequently in children but may be found occasionally in adults—the so-called Ghon's focus, previously described by Parrot. It is usually subpleural and is most frequently in the right upper lobe. Next to be affected are the tracheobronchial glands. Stress is laid on the fact that all shadows at the hilus are not necessarily tuberculous. Primary respiratory infection is discussed at further length in an interesting fashion, but the discussion is too long to be abstracted here.

Types of bacilli are also discussed and are given with their percentages in a table.

*Primary Tuberculosis.*—The author found that in 34 per cent of the cases in his series the portal of entry was in the alimentary tract and that in 2 per cent it was the cervical glands. Primary abdominal tuberculosis is considered, next its incidence, likewise the type of bacilli found at the portal of entry. Primary

tuberculous cervical adenitis is discussed briefly, then the methods, more or less familiar and conventional, of preventing the spread of tuberculosis in general.

ROYSTER, University, Va.

ACTINOMYCOSIS OF THE LUNG. D. PATERSON, Proc. Roy. Soc. Med. **29**:1433 (Sept.) 1936.

A case in a girl aged 9 years is reported. WILLIAMSON, New Orleans.

A TUBERCULOUS CAVITY IN A CHILD OF TEN MONTHS CURED BY PHRENICECTOMY. H. ESCHBACH, Bull. Soc. de pédiat. de Paris **33**:420 (June) 1935.

Collapse therapy is indicated in ulcerative forms of tuberculosis of the lungs in children, as in adults. A boy 9 months old had a large subapical cavity on the left side. When attempts at artificial pneumothorax failed, phrenicectomy was performed. Four years later he was entirely cured and no abnormality of the lung where the cavity had been could be discerned. The diaphragm had recovered some movement, which was still less than normal.

BENJAMIN, Montreal, Canada.

STATISTICS OF CUTANEOUS TUBERCULIN TESTS PERFORMED ON PARISIAN CHILDREN. M. COFFIN, Bull. Soc. de pédiat. de Paris **34**:216 (April) 1936.

Tuberculin tests were done on children from 2 to 16 years old. The details of the procedure (apparently von Pirquet's) are not given nor is it mentioned when the reactions were read. The remark is made that among reactions those marked only by slight redness were called positive as well as those which showed induration. The observations in 370 children are reported. Of 113 positive reactors, definite contact with a tuberculous person was established for only 38.27. Children whose reactions were negative when they were first tested were retested after some time, and in 25 per cent of them, the majority between the ages of 7 and 10 years, the reactions were found to have become positive. Definite contact was traced for a larger percentage (79) of the positive reactors whose parents were regularly examined at a clinic for tuberculous persons. Coffin combined his figures with those of a colleague working along the same lines at another clinic in Paris and shows in tables the number of negative, the number of positive and the percentage of positive reactions obtained at the ages from 2 to 16 years among 1,151 children. The numbers of children who reacted positively are much smaller than those reported in similar studies by other observers in former years, and it is believed that intensive preventive efforts against the spread of tuberculosis account for the significant difference.

BENJAMIN, Montreal, Canada.

MILIARY TUBERCULOSIS WITH BACILLI IN THE GASTRIC CONTENTS: PROGRESSIVE IMPROVEMENT. P. F. ARMAND-DELILLE and J. BOYER, Bull. Soc. de pédiat. de Paris **34**:239 (April) 1936.

A boy 14 years old showed typical miliary tuberculosis in the roentgenologic examination of the chest. Tubercle bacilli were found on one occasion only in stomach washings during fasting, and never in the sputum. The boy did not do well for some time but then began to improve so that his general condition was good enough to allow him to be sent to a sanatorium about four months after he was first observed. A roentgenogram of the chest again showed miliary involvement of both lungs. After five months at the sanatorium, his color was good, he had a good appetite, cough and expectoration had practically subsided, and he was afebrile and had gained 8 Kg. in weight. The onset of the disease resembled grip. The usual typhoid-like period did not occur. The further course time will tell.

BENJAMIN, Montreal, Canada.

TUBERCULIN SENSITIVITY OF CHILDREN RECEIVING SUBCUTANEOUS INJECTIONS OF B C G. ROBERT DEBRÉ, MARCEL LELONG and MLLE. PICTET, Compt. rend. Soc. de biol. **116**:37 (May 5) 1934.

Subcutaneous injections into the thigh or axillary region of 0.03 mg. of B C G, prepared according to the method of the Pasteur Institute, were given to children from 1 to 4 years of age who showed a negative reaction to 1 cg. in the tuberculin test. Locally small lentil-sized nodules formed, without redness or tenderness, and were absorbed without suppuration. Fifty-six per cent of the children gave positive reactions six weeks later, and 43 per cent, mild reactions.

A second group of infants, who had been inoculated shortly after birth, were revaccinated by the subcutaneous route, as in the first group. The tuberculin reactions remained the same as after the first inoculation.

It is believed that the sensitivity produced, as indicated by the tuberculin test, is the same by the subcutaneous route six weeks after inoculation as for those inoculated orally at birth.

WAHL, Cleveland.

PULMONARY TUBERCULOSIS AND CONCEALED TUBERCULOSIS IN SCHOOL CHILDREN. R. ORTEGA, Arch. hosp. de niños Roberto del Rio **5**:113 (Sept.) 1935.

A total of 918 children between the ages of 4 and 15 were studied. The majority of these children belonged to the middle class both socially and financially, as proved by their heights and weights and by social service investigations. The Pirquet (scarification) test was used with a 1:1,000 dilution of old tuberculin. X-ray pictures were taken of the thorax in anteroposterior and lateral oblique positions in every case. Noting of weight and height and examination for enlarged lymph nodes and cutaneous manifestations completed the routine procedure. The investigation disclosed that 61.25 per cent had positive reactions and that 3.79 per cent had evidence of active though mild pulmonary tuberculosis. In the group with concealed disease, the author includes all those who reacted positively to the tuberculin but in whom the x-ray pictures failed to show any evidence of pulmonary involvement and who had no cervical adenitis. These comprised from 50 to 60 per cent of the entire series.

On the basis of these statistics and in consideration of the fact that there are 425,555 children enrolled in the "primary" schools in Chile, there should be over 16,000 children affected with active pulmonary tuberculosis in the country. These would all need medical care and proper attention. Ortega stresses the probability that the percentage among the laboring classes is higher. He terminates his report by making a strong plea for proper consideration of this important problem.

SCHLUTZ, Chicago.

PATHOGENESIS OF SCROFULA. E. CIENFUEGOS, Arch. de pediat., Rio de Janeiro **7**:334 (April) 1936.

Scrofula is probably the infantile expression of resistance to tuberculosis of a toxic nature, manifest in the lymphatic system. It might be considered as a defensive allergic reaction. Other similar manifestations are phlyctenular keratitis, erythema nodosum and epituberculosis.

SANFORD, Chicago.

THE SCHICK TEST—PSEUDOREACTION AND TUBERCULOSIS. H. STARCKE, Arch. f. Kinderh. **108**:31 (April 28) 1936.

The Schick test can become negative because the reaction becomes sluggish. This sluggishness is nonspecific and can be overcome by a second Schick test or by a tuberculin test. Anergy in severe illness, e. g., miliary tuberculosis, affects not only the reaction in the Pirquet but also that in the Schick test in the sense of converting a positive into a negative reaction. A high percentage of the positive reactions in actively immunized children become negative after a sufficient

period. That a like alteration occurs in tuberculous children speaks against the theory that the reaction is influenced by tuberculosis. Tuberculosis affects the Schick reaction only through the positive Pirquet reaction, which can overcome the sluggishness of the Schick reaction. CRANE, Chicago.

A PRACTICAL EVALUATION OF NINNI'S EXPERIMENTAL TUBERCULOSIS WITH A CONTRIBUTION ON THE QUESTION OF THE FREQUENCY OF OPEN PULMONARY TUBERCULOSIS IN CHILDREN WITH POSITIVE REACTIONS TO TUBERCULIN. A. NETRASIRI, Arch. f. Kinderh. **108**:217 (Aug. 4) 1936.

Using Ninni's method, by which material from patients suspected of having tuberculosis is injected into the cervical glands of a guinea-pig and an examination of smears of the glands made after from fourteen to twenty days, the author finds that the examination of the smears is time-consuming and the method not entirely reliable after the shorter period, while it loses its advantage over other methods if the longer period is required.

Stomach washings from forty-four children with positive reactions to tuberculin were proved positive for tubercle bacilli in 25 per cent of the cases. In all eleven cases there was infiltration of the lung. CRANE, Chicago.

CLINICAL RESULTS OF THE CALMETTE PROTECTIVE VACCINATION (BCG). BERTHOLD EPSTEIN, Jahrb. f. Kinderh. **145**:237 (Nov.) 1935.

Following a comprehensive review of the literature, Epstein quotes some of his own work, pointing out differences between his findings and those of others. He makes a plea for more carefully supervised and controlled work. He points out (in agreement with C. A. Stewart and others) that there has been a general decline in morbidity and mortality from tuberculosis. He advises special study of that group of children who are destined to live in tuberculous environments. Until this study is made the efficacy of BCG vaccination will remain in doubt.

LANDAU, Hannibal, Mo.

TREATMENT OF CONGENITAL SYPHILIS WITH ACETARSONE. R. GERTH, Monatschr. f. Kinderh. **67**:46 (Sept.) 1936.

Gerth reports favorable results from the treatment of congenital syphilis in infants with small doses of acetarsone. There is, however, danger of a severe Herxheimer reaction following too large an initial dose. He gives an extensive table showing the varying recommendations of many authors as regards dosage and duration of treatment. His final conclusion is that there is no definite amount for the initial dose of the drug but that one must make a decision accordant to the individual case and then increase cautiously. There is also no classification as yet of the type of congenital syphilis in which the drug is specifically recommended or of the type in which it is contraindicated. GERSTLEY, Chicago.

CONGENITAL BONE SYPHILIS. T. S. JUNG, Chinese M. J. **50**:352 (April) 1936.

The study deals with an analysis by the hospital roentgenologist of the findings in the long bones of sixty-two infants less than a year old who were proved to have congenital syphilis. Jung quotes the classic articles of Wimberger, Pendergrass and Bromer, and McLean. The three types, osteochondritis, periostitis and hypertrophic osteoporosis, form the basis of classification. Osteochondritis usually heals rapidly; periostitis appears last. Signs of healing in the former are observed as early as two weeks after the beginning of treatment. Actual increase in the density of periosteal shadows was observed in some of the instances of healing osteomyelitis. The x-ray films reproduced fill several pages.

NEFF, Kansas City, Mo.

STOVARSOL TREATMENT OF CONGENITAL SYPHILIS IN CHINESE CHILDREN. P. L. FAN, Chinese M. J. **50**:364 (April) 1936.

This report comes from the pediatric division of the school of medicine of Cheeloo University, Shantung. The parental psychology in China is typical of that exhibited in the clinics of America: When acute symptoms in the syphilitic child have disappeared, further observation is usually stopped. Time and distance are factors in the failure to bring the child for continued treatment. Another factor is the unpleasantness of the injections both from the pain produced and from the publicity connected therewith. Fan thinks that oral administration of the drug as used in his work makes treatment much more desirable. He follows the dosage of Bratusch-Marrain, beginning with small doses and gradually increasing the amounts on the basis of the body weight, as being safer. He forewarns parents that symptoms of poisoning, namely, fever, loose stools, vomiting or rash, should be promptly noted, the medicine stopped and the child brought to the clinic. He reports nine cases in detail, tabulating the symptoms and the treatment, and reviews series of cases reported in the literature. Serologic tests following treatment of these small infants are satisfactory. Adequate treatment may result in complete healing of bone lesions.

NEFF, Kansas City, Mo.

TUBERCULOUS MENINGITIS. JUI-PING WU, Chinese M. J. **50**:506 (April) 1936.

During the past fourteen years 447 cases of meningitis in children were observed at the Peiping Union Medical College, and in 216 of these it was tuberculous. The cases were analyzed as to age of patient, mode of onset, physical findings, type of fever and incidence of common signs. Tables are offered on the presence of tuberculous lesions in other parts of the body, the interval between the detection of beginning tuberculosis and the onset of meningitis. In 50 per cent of the cases the white blood cell count was between 10,000 and 20,000, and the percentage of polymorphonuclear leukocytes was practically always high irrespective of the age of the patient or the duration of the disease. The spinal fluid cell count was below 200 per cubic millimeter in half of the cases and was about 500 in approximately 15 per cent of the cases, with marked preponderance of lymphocytes at all ages.

In 69 per cent of the cases tubercle bacilli were isolated. In 65 per cent of the cases pulmonary lesions were found, the miliary type being more frequent in childhood.

NEFF, Kansas City, Mo.

PERCUTANEOUS PLASTER TUBERCULIN TEST IN CHILDREN. MONRAD, Ugesk. f. læger **98**:885 (Sept. 17) 1936.

Monrad gives his experience with a large number of tuberculin tests performed by the plaster, or contact, method controlled by the Mantoux reaction. He states that the contact method is more convenient, and that the reaction is more definite, and he does not hesitate to recommend this method for routine use.

ELGHAMMAR, Chicago.

TUBERCULOSIS IN SCHOOL CHILDREN IN EE AND ON THE ISLE OF TERSCHELLING. J. P. MUNTING, Maandschr. v. kindergeneesk. **5**:295 (April) 1936.

Two groups of children were observed, a group of twenty-four coming to the sanatorium from a school at Ee and a group of eleven from a school on the isle of Terschelling (both in Netherlands). A teacher suffering from open pulmonary tuberculosis had taught in both schools. The lungs of these children showed perihilic infiltrations, sometimes combined with rather extensive infiltrates lying farther in the lung. During the stay of the children at the sanatorium the changes in the lungs of many of them at first still showed distinct progression, and in several children extrapulmonary tuberculous foci developed as well. Attention is drawn to the relative value of the several signs in judging the activity of the

tuberculous process in children; in addition, the necessity of regular roentgenologic control is pointed out. On the whole, the rapidity of sedimentation of the erythrocytes showed more distinct changes than the hemogram. The contents of the stomachs of the twenty-four children from Ee were examined for tubercle bacilli, with positive results in seven.

VAN CREVELD, Amsterdam, Netherlands.

STUDY OF TUBERCLE BACILLI ISOLATED FROM SCHOOL CHILDREN AT EE. H. D. BOER, Maandschr. v. kindergeneesk. **5:** 311 (April) 1936.

Boer describes the tubercle bacilli isolated from the children of Ee, Netherlands, who got their infection from a teacher with open pulmonary tuberculosis. The bacilli had the same characteristics as those isolated from the teacher; e. g., they could be cultured with difficulty on different mediums and formed an orange-colored pigment on potatoes.

VAN CREVELD, Amsterdam, Netherlands.

VIS MEDICATRIX NATURAE. C. DE LANGE, Nederl. tijdschr. v. geneesk. **80:**4436 (Oct. 3) 1936.

A child had been infected with tuberculosis by the mother within the first month of life. Severe pulmonary tuberculosis developed, and a cavernous process in the right lung produced spontaneous pneumothorax at the age of 8 months. The child is now 2 years old, and provisionally one may speak of a recovery.

VAN CREVELD, Amsterdam, Netherlands.

DANGER OF TUBERCULOUS INFECTION OF NURSES IN SANATORIUM SERVICE. P. J. DE BLOEME, Nederl. tijdschr. v. geneesk. **80:**4441 (Oct. 3) 1936.

Bloeme, director of a sanatorium for tuberculous patients, comes to the following conclusions:

1. The protection of nurses against tuberculous infection consists—irrespective of the skin reaction to tuberculin—in measures of strict hygiene, prophylaxis and order throughout. These measures entail special features according to the nature of the institution.

2. B C G vaccination of nurses with negative skin reactions may be of some value when the paramount importance of hygiene is realized. Such vaccination is valueless under unsatisfactory hygienic conditions.

3. A negative skin test does not exclude previous infection; a positive test does not imply artificial immunity. Natural resistance, however vacillating in character, must be valued.

4. Active tuberculosis occurred in 1.05 per cent of 800 nurses during service in the sanatorium.

5. Probationers below the age of 20 should preferably not enter into the service of institutions for the care of tuberculous patients.

VAN CREVELD, Amsterdam, Netherlands.

THE PROBLEM OF A FILTRABLE VIRUS OF TUBERCULOSIS. J. VAN DER LEE, Nederl. tijdschr. v. geneesk. **80:**4458 (Oct. 3) 1936.

The communications on record about the problem of a filtrable virus of tuberculosis are considered unconvincing and contradictory regarding the atypical tuberculosis of experimental animals as well as regarding the opinions about the filtrable virus itself.

VAN CREVELD, Amsterdam, Netherlands.

School Epidemics of Tuberculosis Caused by Open Pulmonary Tuberculosis of Pupils. H. Sandra, Nederl. tijdschr. v. geneesk. **80**:4470 (Oct. 3) 1936.

In connection with some school endemics of tuberculosis reported by the author, the danger that school children with open tuberculosis may communicate their disease to their fellow pupils is pointed out, which danger should not be regarded as less serious than that of tuberculous teachers. Efficacious dealing with this danger, which means prevention, is difficult. Establishment of a school medical service which would include all school children would be of considerable use in this respect.

van Creveld, Amsterdam, Netherlands.

Tuberculosis of the Bronchial Glands After Childhood. M. M. Hijmans, Nederl. tijdschr. v. geneesk. **80**:4477 (Oct. 3) 1936.

Tuberculosis of the bronchial and tracheal glands occurs not only in young but in older children and in adults. The condition in the latter groups is probably caused by activation, through infection with tubercle bacilli, of a focus which developed in the preceding years. In most of the author's patients allergy against tuberculin, estimated by the Pirquet reaction, was weakly positive or negative. The prognosis is generally favorable; rarely, extension into the lung or hematogenous metastasis is met. The diagnosis in almost all cases could be made only by roentgenologic examination, in which fluoroscopic inspection proved to be an invaluable help. This form of tuberculosis does not fit into the well known scheme of the stages of Ranke.

The differential diagnosis has to deal only with lymphadenoma and other neoplasms. The course of the disease in the cases described in this paper proved that these conditions could be excluded.

van Creveld, Amsterdam, Netherlands.

Morphologic Aspects of Tubercle Bacilli. G. Kapsenberg, Nederl. tijdschr. v. geneesk. **80**:4540 (Oct. 3) 1936.

Kapsenberg outlines present views on the morphologic aspects of Mycobacterium tuberculosis. In all probability, if tuberculous material (sputum, spinal fluid, pus) which on microscopic research does not disclose acid-fast bacilli were cultivated directly on a proper medium, it would help to improve knowledge of the different forms which the tubercle bacillus may assume. It happens at times that inoculation of "microscopically negative" material produces such a dense culture that the current explanation, according to which any acid-fast bacilli present would be overlooked, is not tenable. Some examples are given and illustrated by photographs.

Consequently, it seems necessary in the case of microscopically negative material to pay attention also to the unusual forms which may be related to the tubercle bacillus and to compare the results of the microscopic research qualitatively and quantitatively with the cultural results. Löwenstein in his recently published book (1936) has reported similar observations and ideas.

van Creveld, Amsterdam, Netherlands.

## Diseases of Blood, Heart and Blood Vessels and Spleen

Cardiac Hypertrophy in a Case of Cooley's Anemia. G. Nemet and H. Gross, Am. Heart J. **12**:352 (Sept.) 1936.

A case of severe anemia assocated with cardiac hypertrophy is reported. The physiologic factors responsible for cardiac hypertrophy are briefly discussed. An attempt is made to explain the cardiac hypertrophy in this case from a physiologic point of view.

Cardiac hypertrophy is rare in anemia. Since dilatation is usually present in severe anemia, and an initial increase in length may therefore be assumed, some factor other than chronically increased length must be present for cardiac hypertrophy to develop.

From the Authors' Summary.

WIDELY PATENT FORAMEN OVALE: A CASE REPORT WITH DISCUSSION OF DIAGNOSIS. H. TARNOWER and I. O. WOODRUFF, Am. Heart J. **12**:358 (Sept.) 1936.

A case of widely patent foramen ovale in a woman aged 77 is reported, showing the characteristic physical signs, x-ray picture and electrocardiographic changes.

Among the features to be observed in a patient with widely patent foramen ovale, the following may be listed:

1. Delicate physical make-up
2. Cyanosis tardive
3. Physical signs: large heart, prominent conus and unusual signs at the base (not common)
4. Roentgenologic features: small aortic knob, prominent pulmonary conus, wide hilar vessels and enlarged globular heart
5. Electrocardiographic findings: right axis deviation and auricular fibrillation (relatively common)

This case further serves to illustrate the rather benign nature of a large interauricular septal defect if it is unaccompanied by a valvular lesion.

FROM THE AUTHORS' SUMMARY.

ACUTE BACTERIAL ENDOCARDITIS IN INFANTS: REPORT OF A CASE. F. W. MULSOW and H. R. HESS, Am. Heart J. **12**:368 (Sept.) 1936.

A 4 month old infant presented symptoms of sepsis. The blood culture revealed Streptococcus haemolyticus. The physical examination showed the heart to be normal. The diagnosis at autopsy was streptococcic septicemia with petechial hemorrhages in the skin and serous surfaces, infarcts of the spleen and kidneys, ulcerative endocarditis of the aortic valve and enlargement of the glands of the neck. The throat was apparently the source of infection. GIBSON, Chicago.

A CASE OF CONGENITAL AORTIC ATRESIA. J. T. ROBERTS, Am. Heart J. **12**:448 (Oct.) 1936.

In the case reported, congenital aortic atresia was associated with mitral stenosis, hypoplasia of the left ventricle, dilatation and hypertrophy of the right ventricle and pulmonary artery, stenosis of the ascending aorta and arch, patency of the foramen ovale, patency of the ductus arteriosus and defect of the interventricular septum.

The patient died at the age of 20½ hours. Cyanosis became apparent a few hours before birth, and a few hours later dyspnea occurred.

The question whether a prenatal inflammatory condition or an arrest of development was responsible for the aortic atresia is discussed. GIBSON, Chicago.

COMPARATIVE STUDY OF CYTOPLASMIC AND NUCLEAR CHANGES IN NEUTROPHILS IN SEVERE INFECTIOUS STATES. T. H. MENDELL, D. R. MERANZE and T. MERANZE, Am. J. M. Sc. **192**:301 (Sept.) 1936.

Sixty cases of severe infectious diseases have been studied to ascertain the relative clinical value of the degenerative cytoplasmic changes (degenerative index) and the nuclear changes (Schilling index) in polymorphonuclear neutrophils. In twenty of the sixty cases studied, the degenerative index and the Schilling index proved to be of equal value. Of the remaining forty cases, in thirty-six (90 per cent) the degenerative index was superior to the Schilling index. In only four of the forty cases (10 per cent) was the Schilling index superior to the degenerative index.

This series showed that at the height of the illness the degenerative index more accurately reflected the existing clinical state and the subsequent course.

Degenerative cytoplasmic changes appeared earlier and persisted longer than did the corresponding nuclear changes during the critical stages of the illnesses studied. It is important to note how valuable both tests proved to be, and that, though the degenerative index proved to be superior in the majority of cases, the Schilling index again showed itself to be a valuable procedure.

From this study it is again evident that in severe infection no hemogram is complete without determination of the degenerative index.

HENSKE, Omaha.

ACUTE SUPPURATIVE PERICARDITIS. J. H. HEYL, Ann. Surg. **104**:365 (Sept.) 1936.

In 1933 Truesdale listed 152 reported instances of acute suppurative pericarditis in which treatment was by pericardiotomy. The mortality in these cases was 42 per cent.

Heyl believes that this condition is as much a surgical disease as empyema. He reports a case occurring in an 18 month old infant, who is the next to the youngest patient reported and the youngest of the survivors. He gives as cardinal symptoms an increase in the area of cardiac dulness, precordial bulging, a diffuse and wavy apex beat and an area of dulness and bronchial breathing in the left lower part of the chest posteriorly. These signs, accompanied by dyspnea, orthopnea, a septic rise in temperature, a weak rapid pulse, cyanosis and leukocytosis, should suggest the diagnosis.

He discusses the operative technic.

BANTIN, Omaha.

SEVERE MYOCARDITIS OF UNKNOWN ETIOLOGY. H. B. TAUSSIG and E. H. OPPENHEIMER, Bull. Johns Hopkins Hosp. **59**:167 (Sept.) 1936.

The case is one of a child in whom a syphilitic infection developed following intramuscular injections of whole blood. At first she responded well to treatment, and then suddenly, two months later, an eruption of the skin developed and she died of cardiac failure. Autopsy revealed an extensive diffuse myocarditis in which round cell infiltration and tubercle-like proliferative lesions were prominent. There were similar lesions in the lungs, liver and lymph nodes.

Even though the clinical events preceding death made syphilis appear to be the most probable cause of the disease, and the pathologic findings were also consistent with a severe syphilitic infection, the authors were unable to establish the diagnosis. Consequently, although they believe that the disease may have been syphilitic in origin, they think that it is entirely possible that the condition was caused by some other unidentified infectious agent. The case, however, was so remarkable and the lesions so striking that they put it on record in the hope that through reports of similar cases its nature may ultimately be recognized with certainty.

FROM THE AUTHORS' SUMMARY.

GAUCHER'S DISEASE. T. F. BLOEM, J. GROEN and C. POSTMA, Quart. J. Med. **5**:517 (Oct.) 1936.

In addition to the usual clinical findings in the five cases of Gaucher's disease which they report, the authors emphasize the presence of pigmentation of the lower parts of the legs, a malar flush and myopia. Frequently there is an increase in the nitrogen of the blood plasma, with the phosphorus normal.

BRADFORD, Rochester, N. Y.

XANTHOMATOSIS OF THE SKIN AND THE SYNDROME OF HAND-SCHÜLLER-CHRISTIAN. J. R. DREYFUS, Arch. de méd. d. enf. **39**:569 (Sept.) 1936.

Clinical data in the case of a girl under observation in the hospital for two years and eight months are reported. At the age of 1 year, there were noted

xanthelasma of the eyelids and xanthomas of the skin, the latter affecting the regions of the shoulders and the chin and verified by biopsy. Coincident with these dermatologic lesions and in spite of insulin therapy, there were an increase in the cholesterol content of the blood to 290 mg. per hundred cubic centimeters, the computation being made by the Bloor method, and marked retardation in the sedimentation rate.

There was disequilibrium in the metabolism of carbohydrate and probably also in that of the bile pigments; giant cells of a type recently described by Esser were found in every blood smear, and roentgenograms revealed xanthomatous invasion of the pelvic bones.

A diet entirely free from fat resulted in prompt improvement of the cholesteremia and corresponding amelioration of the cutaneous lesions.

AMESSE, Denver.

CONGENITAL HEART DISEASE ASSOCIATED WITH CYANOSIS AND POLYCYTHEMIA. PÉREZ DE LOS REYES, ALVARO SILVA and HORACIO DE LA TORRE, Arch. de med. inf. **5**:263 (Aug.) 1936.

A child aged 7 years had suffered from cyanosis since birth, and later showed clubbing of the fingers. The father died of tuberculosis. The extent of the polycythemia was 8,800,000 red cells. The heart murmur was presystolic, and the authors believe the case may be one of the tetralogy of Fallot.

SANFORD, Chicago.

DEXTROCARDIA ASSOCIATED WITH TOTAL INVERSION OF THE VISCERA. AMERICO AUGUSTO, Arch. de pediat., Rio de Janeiro **7**:435 (July) 1936.

A child 4 years old with dextrocardia associated with total inversion of the viscera had no symptoms. The article is illustrated with roentgenograms and cardiograms, which were reversed.

SANFORD, Chicago.

HIPPOCRATIC FINGERS AND THE BAMBERGER-MARIE SYNDROME. N. QUIRNO, Rev. méd. latino-am. **21**:1383 (Sept.) 1936.

After having enumerated the historic facts, Quirno discusses the pathologic anatomy of hippocratic fingers (clubfingers), especially the vascular changes which are important in the development of this condition. He analyzes the Bamberger-Marie syndrome and insists on the differential characteristics of this disease and simple hippocratic fingers. He comments on the chronological appearance of the symptoms and the possibility of their complete disappearance. Finally, there is a study of the roentgenologic findings in hypertrophic pulmonary osteo-arthropathy.

DWYER, Kansas City, Mo.

CONGENITAL HEART BLOCK. OTTO CAMMANN, Monatschr. f. Kinderh. **66**:278 (Aug.) 1936.

Two cases of congenital heart block are reported, and roentgenograms and electrocardiograms are shown. The prognosis is not to be determined by the electrocardiogram but by the general condition of the child.

GERSTLEY, Chicago.

DIAMETER OF ERYTHROCYTES. JULIAN T. RUBIO, Monatschr. f. Kinderh. **66**:292 (Aug.) 1936.

This article consists of a series of observations and tables giving the diameter of erythrocytes during the various quarters of the first two years and in pathologic conditions such as nutritional disturbances, allergy, tuberculosis, general infections and so forth. The differences are so slight that the findings cannot as yet be of practical importance.

GERSTLEY, Chicago.

ENDOCARDITIS LENTA IN CHILDHOOD. W. WEDEKIND, Monatschr. f. Kinderh. **67**:129 (Oct.) 1936.

Wedekind reports a case of subacute bacterial endocarditis. There was nothing unusual in the history or physical findings to make the case worth reporting.

GERSTLEY, Chicago.

A BROKEN NEEDLE IN THE PERICARDIUM OF A CHILD ONE AND ONE HALF YEARS OF AGE. HANSEN and GRÜNINGER, München. med. Wchnschr. **83**:1513 (Sept. 11) 1936.

A child aged 1½ years became ill with anorexia, irritability, and edema starting in the lower extremities. Later, dyspnea and ascites developed. A tentative diagnosis of nephritis was made, though the urine contained only a trace of albumin. While under observation the area of cardiac dulness increased, and the heart sounds became muffled. Roentgenograms revealed pericarditis, pleural fluid on the left side and a needle apparently in the pericardium on the right side. The child was critically ill but was slightly improved after a thoracentesis in which 115 cc. of fluid was removed. Several days later the pericardium was incised, and the needle, which was partially embedded in the myocardium, was removed. The child made a surprisingly rapid recovery.

After the needle was observed, the mother recalled that a few weeks before she had noted a tender area on the left side of the child's chest. Apparently the needle had penetrated the wall of the chest and finally found its way into the myocardium.

BRAHDY, Mount Vernon, N. Y.

ACCURACY OF HEMATOLOGIC COUNTING METHODS. PREBEN PLUM, Acta med. Scandinav. **90**:342, 1936.

After a brief historical survey of the development of counting methods, Plum, with careful work, proves that the unequal, accidental distribution of cells in counting chambers and smears, and not the measuring of blood and mixing fluid, plays the predominant rôle in the error of the individual count.

The mean error in the counting chamber is equal simply to the square root of the counted number of cells, while the mean error in smears can be calculated according to the Bernoulli theorem.

KAJDI, Baltimore.

INCREASE IN RETICULOCYTES AFTER INJECTION OF "ANEMIC SERUM." ERLING HJORT, Norsk mag. f. lægevidensk. **97**:270, 1936.

Intravenous injection of serum from rabbits just previously bled produced in a third of normal rabbits an increase in the number of reticulocytes. This reaction was similar to that seen after large hemorrhages. In the other two thirds of the rabbits a slight increase or a slight decrease was noticed. Anemic serum from the same rabbit produced in two different animals various reactions; in one a large increase, and in another, just a slight increase or a decrease of the reticulocytes.

When a definite increase in the number of reticulocytes was seen, no similar increase in the red corpuscles was noticed.

TOVERUD, Oslo, Norway.

## Diseases of Nose, Throat and Ear

FREQUENCY AND EFFECT ON EUSTACHIAN TUBE OF RESIDUAL LYMPHOID TISSUE IN THE NASOPHARYNX. D. ROY, Arch. Otolaryng. **24**:325 (Sept.) 1936.

Lymphoid tissue in the nasopharynx is well recognized because of its blocking effect and because it is a source of infection in the middle ear. Lymph follicles have been found in the cartilaginous portion of the eustachian tube and these

are called Gerlach's tonsil or tubal tonsil. A study of such tissue in patients of all ages and the opinions of many authors concerning the tonsil of Gerlach are given.

To obviate the presence of the tubal tonsil, a thorough removal is necessary. Roy has treated remnants in Rosenmüller's fossa, which may extend about the eustachian tube, by chemical cauterization, and he describes the procedure and compares it with other methods of treatment. He concludes that many aural conditions would be permanently benefited if this lymphoid tissue in and around the orifice of the eustachian tube were considered by the laryngologist.

GREENWOOD, Chicago.

OTITIC MENINGITIS: REPORT OF A CASE IN WHICH TREATMENT WITH CONTINUOUS SPINAL DRAINAGE WAS USED. J. POPPER, Arch. Otolaryng. **24:** 340 (Sept.) 1936.

Drainage, either surgical or conservative, is of paramount importance in the management of septic meningitis. The simple lumbar or cisternal puncture done at frequent intervals has been reported to result in cure. Instead of the use of the rigid needle, Popper describes the simple expedient of inserting a ureteral catheter through the lumbar puncture needle and leaving it in place. He reports a case in which the permanent method of drainage was used in the treatment of an infant with meningitis, prolonging the infant's life for twenty-six days after the operation. He concludes that because ordinarily streptococcic meningitis proves fatal within from two to five days the permanent drainage used in this case was important in prolonging life.

GREENWOOD, Chicago.

FOLLOW-UP OF PATIENTS EIGHT MONTHS AFTER TONSILLECTOMY. H. D. SMITH, Arch. Otolaryng. **24:**488 (Oct.) 1936.

In a series of cases the history of the patient whose tonsils have been removed was correlated with the pathologic diagnosis and clinical course over a period of eight months.

The patients who were benefited by removal of suspicious tonsils were those who gave a history of recurrent colds and sore throat, discharging of the ears, nasal blockage, cervical adenitis and hypertrophy of the tonsils. It is doubtful whether those complaining of indigestion, laryngitis or painfulness of the throat were particularly helped.

A comparison of the results is made with those reported by Albert Kaiser over a ten year period. This revealed that the results obtained over the eight month period were more favorable, and Smith concludes that the beneficial effects of the removal of infected tonsils and adenoids gradually decrease after an optimal period of about one year.

GREENWOOD, Chicago.

MYIASIS OF THE LARYNX. A. H. MILLER, Arch. Otolaryng. **24:**501 (Oct.) 1936.

A 6 year old Mexican girl had a cold with high fever for five days, a sore throat the second day and dyspnea the third day. Examination revealed a black ulcerated area of necrotic tissue on the postpharyngeal wall. From this many maggots were seen escaping; the right tonsil was riddled with maggots. After removal of the parasites the patient had several hemorrhages and died after six days. The anatomic diagnosis at autopsy was "necrotic ulceration of the pharynx and larynx due to maggots" that gained entry in spoiled fruit eaten by the child. The condition of atrophic rhinitis probably accounts for the success of the maggots, which attacked already unhealthy tissue. The three types of maggots which infect human beings in the United States are identified.

GREENWOOD, Chicago.

PETROSITIS WITH OPERATION AND RECOVERY. L. KLEINFELD, Arch. Otolaryng. **24**:503 (Oct.) 1936.

Kleinfeld reports the case of a mastoidectomy performed on a boy 9 years old. Subsequent to the operation symptoms developed which led to the diagnosis of suppurative petrositis. A second operation was done, the procedures of which are described, together with the postoperative treatment, with resultant recovery. The author concludes by stating that he has added another report of a case to the literature, has shown the best method of approach and has stressed the significance of the change in the type of pain which occurs when pus breaks through the cortex, namely, an abrupt change from the characteristic ocular pain to a steady throbbing pain in the frontal area.

GREENWOOD, Chicago.

ACUTE AND CHRONIC OTITIS MEDIA, SINUS THROMBOSIS AND SUPPURATION OF THE PETROUS PYRAMID. S. J. KOPETZKY, Arch. Otolaryng. **24**:505 (Oct.) 1936.

Kopetzky first deals with the fundamentals, citing work done in histologic examinations of Shrapnell's membrane, investigations made on nerves, ganglions and the lining of the middle ear in rats and guinea-pigs, and roentgenologic studies of the process of pneumatization in children.

He then discusses acute purulent otitis media, citing reports in the literature of cases in which this condition followed scarlet fever, diphtheria, malnutrition and infections of the middle ear, the latter condition being found for the most part in infants. He states that acute hemorrhagic nephritis may often complicate an infection of the middle ear and that in several cases mydriasis and widening of the palpebral fissure have been reported as complications.

He next deals with chronic purulent otitis media, giving the causes, the findings and the different types of therapy used in treating it, and discusses hearing acuity after radical mastoidectomy.

He cites reports of cases of sinus thrombosis and discusses the treatment followed in these cases.

The anatomic, pathologic and clinical data found in the literature on the petrous pyramid are reviewed. These concern disturbances in the process of pneumatization, the development of Gradenigo's syndrome and the causes of this complication, and are based on studies of clinical cases, x-ray pictures, autopsy material and surgical findings. Lastly, cases of petrositis with complications are cited, and pathways of approach are outlined.

GREENWOOD, Chicago.

THE HARD OF HEARING CHILD. A. J. HOFSOMMER, J. A. M. A. **107**:648 (Aug. 20) 1936.

The hard of hearing child should not be segregated from the public school classroom. Lip reading should be a part of the curriculum. In the majority of instances the intelligence quotient of such a child is low because of lack of educational experience, not because of deficiency in mentality. A study of a group given training in lip reading revealed that 47 per cent showed an increase in the intelligence quotient. In 76.4 per cent there was definite classroom improvement and betterment in behavior. In contrast a group which refused reading, showed no increase in the intelligence quotient, and 75 per cent showed a drop. The education of the unassisted hard of hearing child is an interrupted learning and thus an imperfect acquisition of knowledge.

BONAR, Salt Lake City.

TONSILLECTOMY PERFORMED IN THE OFFICE. F. F. SCHWARTZ, M. Rec. **144**:372 (Oct. 21) 1936.

Schwartz discusses briefly the functions of the tonsil. He had performed tonsillectomy on 260 patients in his office, the ages of the patients varying from 4 to 68 years. He describes the technic used. In conclusion he states that tonsil-

lectomy can be performed in the office very safely and very economically for the patient. The patient consents more readily to the operation since it is "only an office procedure."

WILLIAMSON, New Orleans.

AUDIOMETRIC STUDIES ON SCHOOL CHILDREN. A. CIOCCO, Pub. Health Rep. **51**: 1402 (Oct. 9) 1936.

In Washington, D. C., examination of 14,000 school children with the 4-A audiometer revealed that the results obtained on the children with the best hearing showed the least variation, that the results obtained on boys and those on girls were equally consistent, that the results obtained on high school students were less variable than those on grade school students and that a similar statement is true of the results for the children of higher intelligence. With the 4-A audiometer, loss of 12 sensation units does not indicate significant pathologic change, but loss of 15 sensation units does. Ciocco believes that tests made with the instrument mentioned are inadequate.

SANFORD, Chicago.

ACUTE STREPTOCOCCAL INFECTION OF THE MIDDLE EAR. W. M. MOLLISON, Brit. M. J. **2**:615 (Sept. 26) 1936.

It is thought, I presume, by the author that very seldom is an infection carried to the middle ear by way of the eustachian tube as a consequence of bacteria being blown into the tube. The commonest cause is an acute infection of the whole upper respiratory tract. Acute infection of the middle ear following bathing in fresh water, he thinks, is due to dilution of the mucus by the fresh water, mucus being considered by him and others as protective and as mildly antiseptic. His treatment is outlined.

ROYSTER, University, Va.

ACUTE STREPTOCOCCAL INFECTION OF THE THROAT. E. D. D. DAVIS, Brit. M. J. **2**:617 (Sept. 26) 1936.

This is the second paper in the symposium. Davis gives the various names under which this condition has been known. The subdivisions depend on degree. The first is tonsillitis, with much variation in the extension of the inflammation and edema to the surrounding tissues. The second is gangrenous inflammation, with a sloughing membranous exudate and marked toxemia. This may begin as acute tonsillitis and extend to the more severe condition. Under symptomatology Davis mentions the fulminant conditions, accompanied by edema involving the epiglottis and arytenoids, with difficult swallowing, even inability to swallow saliva. Primary streptococcic laryngitis is rare; cervical adenitis is always present. Ludwig's angina may be a complication and may lead to suppuration. He thinks that if tonsils have been removed previously, both the inflammation of the pharynx and the adenitis are more marked, but both may appear even when the tonsils have not been removed. The most common cause is Streptococcus haemolyticus; other organisms may complicate the picture. Even the pneumococcus alone is sometimes found as a complication. The causal factors in epidemics are discussed. Under treatment he discusses careful, skilful nursing. Careful bacteriologic study, blood transfusions and immunizing blood transfusions may be necessary. Antiscarlatinal streptococcic serum should be given in large doses in streptococcic infections. Antidiphtheritic serum may be of value even when the Klebs-Löffler bacillus is absent and never of value in the presence of a pneumococcus. Neither does the antistreptococcic serum do any good when there is pneumococcic involvement. Suitable types of pneumococcic serum may be used. Davis stresses purgation with mild mercurous chloride; gargles are of little value. Swabbing with hydrogen peroxide and then spraying with a mild antiseptic are thought to be good. Sleep must be induced with powder of ipecac and opium or some other hypnotic. Hot applications are made to the neck in the form of electric heating and inhalation of steam. Potassium chlorate has its value. Fluids

administered by mouth and dextrose injected intravenously are of undoubted benefit. Complications should be treated as they arise. Tonsillectomy should not be performed during the acute stage. When hemorrhage results from a tonsillar abscess tonsillectomy may be necessary. Cervical adenitis should not be treated by incision early. Tracheotomy is indicated in edema of the glottis.

ROYSTER, University, Va.

UNUSUAL FOREIGN BODY IN TRACHEA. A. B. SMITH, Brit. M. J. **2**:715 (Oct. 10) 1936.

The foreign body in the trachea was a piece of egg-shell.

ROYSTER, University, Va.

ETHMOIDAL SUPPURATION WITH ORBITAL INVOLVEMENT. D. PATERSON, Proc. Roy. Soc. Med. **29**:1435 (Sept.) 1936.

Five weeks before the patient, a girl of 2 years, was admitted to the hospital she had contracted measles and had been listless and in poor health since. A week before admission she had become acutely ill with severe pain in her forehead and attacks of shivering. About the fourth day of the illness, puffiness and redness of the right upper eyelid occurred. The next day the eyelid became markedly swollen and the palpebral fissure obliterated. The clinical examination, the progress before operation, the operation, the progress after operation and the investigations are given in detail.

WILLIAMSON, New Orleans.

ACUTE ANGINA IN CHILDREN AND ITS CURE BY BISMUTH (METHOD OF ARISTIDES MONTEIRO). VAZ DE MELLO, Jahrb. f. Kinderh. **145**:203 (Oct.) 1935.

In the department of pediatrics of the Polyclinic of Missao da Cruz, Rio de Janeiro intramuscular injections of bismuth preparations were used in the treatment of nonspecific angina. The preparations were identical with those used in the treatment of syphilis. The dose given was much smaller than that used in antisyphilitic treatment, sometimes 1 mg. per kilogram being sufficient in contrast with 4 mg. per kilogram for antisyphilitic treatment. This dose may be repeated.

The contrast with the results obtained prior to the use of bismuth are remarkable, the author states. Good results are reported in 130 of 131 cases. Often there was a lessening in the severity of the symptoms within from twenty-four to forty-eight hours in contrast with the usual prolonged course.

LANDAU, Hannibal, Mo.

TONSILLECTOMY IN PERITONSILLAR ABSCESSES. C. E. BENJAMINS and E. HUIZINGA, Nederl. tijdschr. v. geneesk. **80**:3853 (Aug. 22) 1936.

The various ways of treatment of peritonsillar abscesses are discussed; tonsillectomy *à chaud,* incision and delayed tonsillectomy *à froid,* and as an intermediate measure tonsillectomy *à tiède,* the most recent method. With the last method very favorable results have been obtained in twenty-one patients. The merits of this method are pointed out, the only disadvantage being that the operation can be performed only on one side at a time. In this respect, attention is drawn to a very important investigation from a theoretical point of view, made by Gangl-Battig (*Ztschr. f. Hals-, Nasen- u. Ohrenh.* **34**:444, 1933).

VAN CREVELD, Amsterdam, Netherlands.

MASTOIDITIS DUPLEX AND CRYPTOGENIC FEVER. H. COHEN, Nederl. tijdschr. v geneesk. **80**:3953 (Aug. 29) 1936.

This communication concerns a case of mastoiditis purulenta involving both ears in a girl of 2 years with no local symptoms pointing to the mastoid, with

no discharge from the ears but with high septic fever. After trepanation and opening of both antrums in one session four weeks after the beginning of the disease, complete recovery followed.

VAN CREVELD, Amsterdam, Netherlands.

OTITIS AND TOXICOSIS IN INFANTS. A. TEN BOKKEL HUININK, Nederl. tijdschr. v. geneesk. **80**: 4874 (Oct. 31) 1936.

A girl of 4½ months showed acute dyspepsia and high fever for six days. Her general condition was bad. The blood picture was highly toxic. Repeated paracentesis, performed without proper indication, had no result. As the condition was hopeless, both antrums were opened; mucopus with diplococci was found on both sides. Three hours later there was beginning of an undisturbed recovery. The author observed ten analogous cases. In each case the desperate condition of the child justified the mastoid operation. Six recovered; the other children died.

VAN CREVELD, Amsterdam, Netherlands.

## Diseases of Lungs, Pleura and Mediastinum

A TEN YEAR STUDY OF EMPYEMA IN CHILDREN—1926-1936. G. C. PENBERTHY and C. D. BENSON, Ann. Surg. **104**:579 (Oct.) 1936.

A certain procedure of treatment has been uniformly followed by the authors. Aspiration is used up to the stage at which frank pus is obtained. At this time the trocar-cannula-catheter method of closed drainage is instituted under local anesthesia. The cavity is aspirated in the operating room until reflex coughing or a small amount of blood-tinged pus appears in the fluid. The patient is then returned to the ward, where further aspirations are carried out every four hours.

The mortality from empyema bears a definite relationship to the type or virulence of the preceding pneumonia and to the age and the general nutrition of the patient.

BANTIN, Omaha.

ACUTE EMPYEMA AS A COMPLICATION IN CONTAGIOUS DISEASES. F. E. BARTON, Arch. Pediat. **53**:654 (Oct.) 1936.

Acute empyema occurred in 16 of 4,589 cases of contagious disease. The operation of choice in all sixteen cases was closed thoracotomy. Two of the patients died—a mortality of 12 per cent.

When the fluid was not encapsulated, Barton selected the posterior axillary line at the most dependent part of the pleural cavity as the site of operation. When the patient's temperature, pulse and blood count were normal, the catheter was removed, provided that the drainage consisted of not more than from 10 to 20 cc. daily and provided that on irrigation it was impossible to instil more than the amount of the daily drainage.

ORR, Buffalo.

EXPERIMENTAL PULMONARY ABSCESS. C. WEISS, A. GOLDMAN and M. C. SHEVKY, Arch. Surg. **33**:649 (Oct.) 1936.

The authors were able to produce pulmonary abscesses in several dogs by introducing the infectious material into the bronchi. The variation in the results was due to difference in the types of organisms introduced and in the natural resistance of the animals. With a hemolytic strain of Staphylococcus aureus, acute abscesses of the lung were produced in a high percentage of the dogs. It was concluded from these experiments that in certain cases pulmonary abscess may be due to aspiration into the lung of infectious material from the upper respiratory passages.

KAISER, Rochester, N. Y.

INTERPRETATION OF HILUS SHADOWS IN CHEST X-RAY OF CHILDREN. J. A. BIGLER, Illinois M. J. **70**:338 (Oct.) 1936.

At the Children's Memorial Hospital, Chicago, during the past ten years postmortem roentgen films have been taken of the lungs. At necropsy a careful comparison has been made of the pathologic picture present on the postmortem films as well as of that on the films taken during life. It is from that experience that Bigler has collected the material for this paper.

His findings are too comprehensive and detailed for adequate abstracting. Among the salient points given are: By a comparison of roentgenograms of excised lungs taken before and after injection of an opaque material into the blood vessels and bronchi it has been found that a large portion of the shadows at the hilus is made up of blood vessels. These are often interpreted erroneously as lymph nodes, as calcified areas or as the beading and studding of tubercles. Lymph nodes if they enlarge may become visible as mediastinal shadows; caseation in itself does not cause lymph nodes to become visible, but when they contain calcium they are easily recognizable. As the shadows at the hilus are made up of a summation of the shadows of the blood vessels, bronchi, lymph nodes and lung tissue, they will vary greatly according to the patient's age. A normal hilar shadow in a child is different from that seen in an older child, a young adult or an aged person. The hilar shadow of tuberculosis is usually triangular, with the base superimposed on the median shadow and the apex reaching into the pulmonary field. A calcified area casts a definite shadow, which is usually easily recognized. When present in and about the hilus this shadow is practically always one of a healed or healing tuberculous lymph node.

Enlargement of the hilus or mediastinum due to noninflammatory pathologic processes is not uncommon in children. Conditions frequently encountered are enlargement of the thymus, Hodgkin's disease, leukemia and malignant tumors. Practically all acute infections of the lower respiratory tract produce changes in the hilar shadows. It is often impossible to differentiate these from the changes evoked by such conditions as central pneumonia and tuberculosis except by consecutive films. In chronic infections there is marked increase in the size and density of the trunk shadows radiating out from the hilus. Pronounced changes take place in the hilar shadow when bronchiectasis is present. Emphysema of the lung as found in asthma may produce a decrease of the density of the hilar shadow because of the increase of air in the alveoli.

BARBOUR, Peoria, Ill.

EPIDEMIC RESPIRATORY DISEASES IN EARLY LIFE. S. J. WILKINSON, Illinois M. J. **70**:348 (Oct.) 1936.

This article consists of observations made by Wilkinson during a five year clinical study of epidemic respiratory diseases in a group of infants and children. Four of the epidemics were apparently initiated by generalized influenza. Other epidemics could not be associated with precipitating factors, although the clinical features of summer epidemics were suggestive of poliomyelitis. The clinical variations in epidemics, especially noteworthy in the influenzal group, suggest that acute respiratory diseases will eventually be recognized in terms of the specifically involved secondary invader. Clinically there were suggestions of characteristic syndromes in different epidemics, possibly related to the various bacterial invaders in acute respiratory diseases. In addition to epidemic variations, marked individual variability was encountered in identical epidemics.

BARBOUR, Peoria, Ill.

EMPYEMA IN INFANTS AND CHILDREN: THE PEDIATRICIAN'S VIEWPOINT. M. GLEICH, M. Rec. **144**:368 (Oct. 21) 1936.

In his summary Gleich states that a study of thirty-five cases of empyema in infants and children over a period of five years teaches the following:

1. Therapeutic aspirations are of value because they enable the child to recuperate from the pneumonia and allow the pus to thicken and be walled off.

2. Therapeutic aspirations occasionally eliminate operations, especially in cases of encapsulated fluid, avirulent organisms and thin seropurulent effusions.

3. Most patients with empyema come to operation, regardless of the time spent in aspirating.

4. Therapeutic aspirations account for a low death rate. The improved methods of operating also must be considered.

5. Pediatricians should stress the value of aspirations as a means of lessening the urgency of operations but not as a substitute for them.

6. Empyema caused by anaerobes needs immediate attention.

7. Get children home as quickly as possible.

WILLIAMSON, New Orleans.

A NEW RAPID METHOD FOR DIRECT TYPING OF PNEUMOCOCCUS IN SPUTUM OF PNEUMONIA CASES. S. J. KLEIN and G. HELLER, Proc. Soc. Exper. Biol. & Med. **34**:488 (May) 1936.

Klein and Heller recommend the use of a 10 per cent solution of saponin in saline solution for dissolving the bacteria and aluminum hydroxide for clarifying the sputum in the typing of pneumococci in lobar pneumonia. Correct typing in twenty of twenty-two unselected cases was obtained with this technic.

HANSEN, Minneapolis.

REMARKS UPON THE SYMPTOM OF COUGH IN RELATION TO CHRONIC AND ACUTE ILLNESS IN CHILDHOOD. C. MCNEIL, Edinburgh M. J. **43**:609 (Oct.) 1936.

This, the sixth paper in McNeil's "Clinical Recollections and Reflections," begins by defining coughing as the removal of sputum from the respiratory organs of the thorax into the throat. Under 7 years of age, children swallow the expectorated material, so that it can be said that "children expectorate but do not spit." In whooping cough and bronchiectasis coughing carries the sputum through the pharynx into the mouth.

McNeil discusses various types of cough and chronic respiratory diseases, among them nasopharyngeal catarrh, bronchiectasis and tuberculous disease of the lungs and mediastinal glands. In nasopharyngeal catarrh the cough is loose, quiet and short, an effort by which mucus is collected into the pharynx and then swallowed. During the daytime such a cough would be overlooked, but at night, when the child is recumbent, mucopurulent sputum can easily be seen on the pharyngeal wall, and the mucous membranes are swollen and slightly reddened. At night the cough is more frequent and occurs in small bouts, which may be associated with laryngeal and tracheal catarrh. The cough of bronchiectasis is characteristic, being paroxysmal, with varying intervals of freedom. In the early morning hours the child may be awakened and caused to sit up by severe bouts of violent coughing, at the end of which sputum is discharged into the mouth in amounts varying from 1 teaspoonful to 1 ounce (31 cc.). Violent exercise during the day may produce a paroxysm, as will also a fit of crying or the swallowing of food. The writer mentions the coexistence of infection of the tonsils and accessory sinuses as a factor which must be taken into consideration. Cough may be absent in tuberculous pulmonary disease in children, though present in children who have progressive and open lesions; as a symptom, it is not of much help in diagnosis.

In the discussion of cough in acute respiratory disease, McNeil includes lobar pneumonia, bronchopneumonia and bronchitis especially. Cough is only a minor symptom in lobar pneumonia, but it is of value in drawing attention to the lungs.

In bronchopneumonia cough is a much more prominent and early symptom, occurring in short bouts and with a harsh quality, often accompanied by definite cyanosis. The cough is similar to that of bronchitis, the general symptoms of the latter disease being less serious.

The author does not go into the subject of treatment.

NEFF, Kansas City, Mo.

PNEUMOTHORAX AND BRONCHIAL COLLAPSE FOLLOWING A CHEST INJURY. W. SHELDON, Proc. Roy. Soc. Med. **29**:1437 (Sept.) 1936.

The case reported occurred in a girl of 9 years who was knocked down by a motor car. The wheel was said to have passed over her chest. The pulse rate was 160. There was surgical emphysema of the front of the chest and of the neck and face up to the eyes, also signs of pneumothorax on the right side. Roentgenograms showed fracture of the right third and fourth ribs, pneumothorax on the right side and the heart displaced to the left. Notes on the progress and reports of roentgen examinations at various dates follow. Reproductions of x-ray plates taken at various stages of the illness accompany the report.

WILLIAMSON, New Orleans.

DETERMINATION OF THE TYPE OR GROUP OF PNEUMOCOCCUS IN INFANTILE PNEUMONIA. A. DORDI, Clin. pediat. **18**:599 (Oct.) 1936.

This is a discussion of the incidence of the various types of pneumococci in thirty-one cases of pneumonia in children. The various members of group IV are not differentiated. The findings in this small case material do not differ from those presented in the numerous published reports on large numbers of cases in the literature.

DOOLEY, New York.

NONTUBERCULOUS SPONTANEOUS PNEUMOTHORAX IN A CHILD. I. TOMA, Spitalul **56**:391 (Oct.) 1936.

Spontaneous nontuberculous pneumothorax is more frequent than tuberculous, although in the French and German literature reports of cases are few. Toma has had occasion to treat, in the pediatric clinic of Cluj, Rumania, a child of 18 months with spontaneous nontuberculous pneumothorax, as diagnosed by physical, roentgenologic and biologic examination. Seven months before, the child had suffered from bronchopneumonia. Because of the grave, almost suffocative condition of the child, Toma was forced to evacuate the air from the pleural cavity. After twenty-one days of treatment, the child recovered.

FROM THE AUTHOR'S SUMMARY.

ARTIFICIAL PNEUMOTHORAX THROUGH A PIERCING WOUND OF THE BRONCHUS CAUSED BY A TACK. C. E. BENJAMINS, Nederl. tijdschr. v. geneesk. **80**:4712 (Oct. 17) 1936.

An upholsterer's tack was aspirated into the right bronchus by a 5 year old girl. After three months roentgenograms revealed that the entire lower and the middle lobe of the right lung had become atelectatic and that the point of the tack had probably pierced the bronchial wall. The tack was removed by inferior bronchoscopy and immediately after its removal cutaneous emphysema announced the foreseen calamity of mediastinal emphysema. An artificial pneumothorax had been prepared for her and was immediately carried out. This excluded the right lung, thus preventing air from penetrating the mediastinum. The child recovered. Half a year after the operation roentgenographic examination revealed shriveling of the entire lower lobe of the right lung, together with bronchiectasis. The child was quite well, however, and had gained considerably in weight.

VAN CREVELD, Amsterdam, Netherlands.

## Diseases of the Gastro-Intestinal Tract, Liver and Peritoneum

EFFECT OF ACETYLSALICYLIC ACID UPON GASTRIC ACTIVITY AND THE MODIFYING ACTION OF CALCIUM GLUCONATE AND SODIUM BICARBONATE. J. G. SCHNEDORF, W. B. BRADLEY and A. C. IVY, Am. J. Digest. Dis. & Nutrition **3**:239 (June) 1936.

Experiments were carried out on normal human subjects, normal dogs and dogs with pouches of the entire stomach.

Ten human subjects were given single doses of: (1) acetylsalicylic acid, (2) a mixture of acetylsalicylic acid and calcium gluconate and (3) a mixture of acetylsalicylic acid and sodium bicarbonate. These subjects had fasted for twelve hours before fractional gastric analysis was conducted on them.

The normal dogs used fasted, and then the stomachs were washed out with distilled water. Control determinations were made by introducing 250 cc. of distilled water and aspirating in twenty minutes; then 250 cc. of an aqueous solution of acetylsalicylic acid or of acetylsalicylic acid and sodium bicarbonate or of acetylsalicylic acid and calcium gluconate was introduced. The volume aspirated at the end of twenty minutes was noted, and determinations of titratable acidity and chlorides were made.

In the dogs with pouches of the total stomach, the stomach pouch was washed with distilled water and a control perfusion was made with 100 cc. of distilled water for one hour. The gastric juice was then collected for two periods of one hour each, after which the pouch was washed and perfused for one hour with 100 cc. of an aqueous solution of acetylsalicylic acid or of acetylsalicylic acid and calcium gulconate or of acetylsalicylic acid and sodium bicarbonate. Following this the gastric secretion was collected again for two one hour periods. The one hour perfusates were analyzed for titratable acidity and chlorides.

The results in normal human subjects and normal dogs may be summed up as follows: 1. Single oral doses of from 1 to 2 Gm. of acetylsalicylic acid caused gastric retention; the addition of calcium gluconate tended to increase the degree of retention, while the addition of sodium bicarbonate increased the rate of gastric evacuation. 2. Single oral doses of acetylsalicylic acid increased the total titratable acidity of the stomach contents; the addition of calcium gluconate diminished the rise in acidity, while the addition of sodium bicarbonate decreased the acidity of the contents below that of the controls. 3. In dogs with pouches of the entire stomach, the local application of acetylsalicylic acid caused a definite increase in the neutral chloride or diluting secretion of the stomach; the addition of calcium gluconate resulted in only a slight increase in the diluting secretion, while the addition of sodium bicarbonate to the acetylsalicylic acid also resulted in only a slight increase in the diluting secretion. None of the solutions increased the formation of hydrochloric acid significantly. 4. Prolonged daily administration of acetylsalicylic acid to normal dogs and to dogs with Pavlov stomach pouches resulted in definite augmentation of the gastric secretion. With the addition of calcium gluconate the increase was not nearly so marked, while sodium bicarbonate and acetylsalicylic acid actually caused a decrease in the gastric secretion below the control values. 5. The neutralizing and inhibiting actions of sodium bicarbonate and calcium gluconate on the titratable acidity of the gastric contents and on the output of hydrochloric acid under the conditions of the experiment may play a definite rôle in the ameliorating effects of these substances on the degree of gastric irritation and the incidence of ulceration produced by prolonged oral administration of acetylsalicylic acid to dogs. Whereas the protective action of sodium bicarbonate may be adequately explained by the reduction of acid irritation, this is not true of the protective action of calcium gluconate against digestive disturbances, which appear to be due in part also to some systemic action of calcium. 6. From the evidence available, it appears that salicylates when given in large doses should be administered with sodium bicarbonate and calcium gluconate.

MORRISON, Savannah, Ga.

INTRA-ABDOMINAL TORSION OF THE APPENDICES EPIPLOICAE, WITH REPORT OF TWO CASES AND REVIEW OF THE LITERATURE. F. A. FISKE, Am. J. M. Sc. **192**:354 (Sept.) 1936.

The appendices epiploicae occur along the entire colon from the cecum to the rectum. They have been described as pouches or processes of peritoneum, and they contain a variable amount of fat, usually considerable in obese persons. The physiologic function of the appendices epiploicae is not clearly understood. Their pathologic changes are chiefly due to mechanical interference with their blood supply or to inflammation.

Fiske feels that intra-abdominal torsion and hemorrhagic infarction of the appendices epiploicae are definite clinical entities. To the cases found in the literature, he adds two, making a total of forty-four. The most characteristic clinical symptom is abdominal pain, usually occurring over the site of the lesion. There may be associated localized tenderness. Nausea and vomiting are uncommon. A palpable tumor was present in seven cases. Preoperative diagnosis is difficult. In any case of obscure abdominal pain which is not explained by operative findings, an exploration of the appendices epiploicae should be considered.

HENSKE, Omaha.

INFANTILE INFECTIOUS HEPATITIS. LEO F. BLEYER and GEORGE R. MURPHY, Arch. Pediat. **53**:43 (Jan.) 1936.

A histopathologic picture is described which Bleyer and Murphy call infantile infectious hepatitis. Clinical and laboratory findings in eight cases are given. While the clinical aspects of the eight cases varied widely, "a review of the hematological and histological data showed a typical response of the infantile organism to infectious-toxic stimuli regardless of their type. This infantile reaction was dominated (1) by marked leukopoietic activity of the liver, associated with more or less invasion of the acini with pus cells, formation of scattered miliary abscesses, periportal infiltration with inflammatory cells of the myelogenous and lymphatic series, and more or less albuminous and fatty degeneration of liver cell columns; (2) by reticuloendothelial proliferation of the spleen and marked venous engorgement of pulp and sinuses; (3) by a marked reaction of the myelogenous or lymphatic . . system manifesting itself in the peripheral blood and associated with hypochromic anemia. [Two cases] differed from the others by development of marked jaundice."

WADDELL JR., Unversity, Va.

OXYURIS VERMICULARIS AND APPENDICITIS. M. A. BELL, Arch. Pediat. **53**:649 (Oct.) 1936.

Oxyuris infestation of the appendix was found in 15 of 138 consecutive cases of appendicitis—an incidence of 10.9 per cent. No oxyurids were found in gangrenous or suppurative appendixes. Chronic or acute catarrhal appendicitis accounted for the symptoms in 84 of the cases. Oxyurids were found only in the latter group, in which the incidence was 17.8 per cent. Eleven of the 15 cases were in females—a ratio of almost 3 to 1.

Oxyuris vermicularis in the appendix will not as a rule produce serious pathologic changes but may give rise to a definite train of symptoms, notably cramplike pain in the region of the appendix, nausea and occasional vomiting. Relief of symptoms occurs if oxyurids are found in the removed appendix. The surgeon should examine the excised appendix at the close of the operation.

ORR, Buffalo.

PRIMARY STREPTOCOCCIC PERITONITIS. L. H. POLLOCK, Arch. Surg. **33**:714 (Oct.) 1936.

An analysis was made of forty-two cases, most of them occurring in infants and young children. The abdominal symptoms generally followed an infection of

the upper respiratory tract. Distention was usually the first abdominal sign, and in half of the cases vomiting occurred. Diarrhea, constipation and abdominal pain were noted in some patients, but this was not a constant complaint. In the majority of instances the abdomen was diffusely enlarged and tender. Evidence of fluid was sometimes elicited. Abdominal puncture was performed on thirty patients and yielded conclusive evidence of the underlying pathologic process in all. With one exception, all of the specimens of fluid obtained on paracentesis yielded pure cultures of Streptococcus haemolyticus (beta). The mortality in this series was 80 per cent. The treatment depended on the severity and stage of the illness. Only in the cases in which the general infection was not marked and there was evidence of much peritoneal fluid was drainage advocated. For the other cases, supportive treatment was used; i. e., a continuous intravenous drip of saline solution, repeated transfusions of blood and an injection of pooled anti-streptococcus serums.

KAISER, Rochester, N. Y.

INJURIES TO THE ESOPHAGUS. C. D. SNELLER, Illinois M. J. **70**:325 (Oct.) 1936.

This paper is based on the records of 100 consecutive cases of esophageal injury from the author's private practice. Fourteen case reports are given to illustrate his experiences. From his study and analysis of the 100 cases he concludes that knowledge of the anatomic structure and of the relationships of the esophagus is essential for interpretation of the symptoms in injuries of the esophagus. The symptoms increase in severity with increase in the severity of the lesion. In 40 per cent of the cases the injury was found at the upper thoracic orifice. Vomiting of acid gastric juices complicates the injury to the esophagus. Blind bougienage and forceful ramming of foreign bodies are to be condemned. All cases of persisting esophageal symptoms should receive careful study by means of the x-ray and the esophagoscope.

BARBOUR, Peoria, Ill.

STAPHYLOCOCCUS FOOD POISONING: REPORT OF A SMALL MILK-BORNE EPIDEMIC. H. J. SHAUGHNESSY and T. C. GRUBB, J. Infect. Dis. **58**:318 (May-June) 1936.

An investigation of a small epidemic of food poisoning involving some twenty-five persons is described. There was little doubt that the consumption of raw milk from cows with staphylococcic mastitis was the cause of the poisoning. The investigation produced the most convincing circumstantial evidence thus far recorded that ice cream may also serve as a vehicle for enterotoxic substances produced by staphylococci. "A hemolytic staphylococcus of the albus variety was isolated from the incriminated milk which, under suitable laboratory cultivation, produced a toxic substance capable of causing vomiting in monkeys and man. It appears probable, therefore, that the cause of the food poisoning was the consumption of milk or ice cream containing a gastro-intestinal irritant elaborated by one and perhaps other strains of staphylococci isolated from the milk. It seems possible that if the recently described technical methods for determining the ability of micro-organisms to produce an enterotoxin are utilized on streptococci and staphylococci from infected udders, mastitis milk may not appear so innocuous as formerly supposed."

TOOMEY, Cleveland.

EARLY DIAGNOSIS OF ACUTE APPENDICITIS. D. O. RHAME JR., J. South Carolina M. A. **32**:233 (Oct.) 1936.

Emphasis is laid on early diagnosis of appendicitis. The first manifestation is pain, which varies in character. Following the pain are nausea, vomiting, fever and leukocytosis. Careful inspection of the abdomen is necessary. The author warns against administration of opiates and laxatives and against delay.

OBERTON JR., Columbia, S. C.

ACUTE INTUSSUSCEPTION IN INFANCY AND CHILDHOOD. C. W. MCLAUGHLIN JR., Nebraska M. J. **21**:333 (Sept.) 1936.

Intussusception is responsible for acute intestinal obstruction in from 60 to 75 per cent of all the cases in infancy and childhood. Of acute abdominal surgical emergencies in infancy and childhood, intussusception is the most common in children under the age of 2. It is encountered more frequently in male babies. They are usually well nourished and in good health. The etiology is not always apparent. Meckel's diverticuli, polyps and intestinal new growth have been found. A local point of irritation or inflamed tissue, possibly some error in the splanchnic nervous system, abnormal mobility of the ascending colon, disproportionate growth of the colon and ileum and irregular action of the intestinal musculature are suggested as etiologic factors. The classic findings are discussed: sudden acute abdominal pain, shock, vomiting, a sausage-shaped abdominal tumor and bloody mucus in the stools. The peculiar emptiness of the right side of the abdominal cavity (sign of Dance) is pointed out. Attention is called to the fact that inability to palpate an abdominal tumor does not necessarily rule out intussusception. It may be obscured by the relatively large liver of the infant. Appendicitis, enterocolitis, rectal prolapse and Henoch's purpura are considered in differential diagnosis. Prompt operative intervention is the only therapeutic measure worthy of consideration. Early diagnosis would lower the mortality.

HAMILTON, Omaha.

ACUTE APPENDICITIS IN CHILDREN. J. SIGNORELLI, New Orleans M. & S. J. **9**:157 (Oct.) 1936.

Appendicitis in childhood is pointed out as frequent and increasingly frequent. It carries an undeservedly high mortality, chiefly because of errors in judgment. The diagnosis is less easy in children than in adults because of the many variations from the classic picture seen in adults. Every case of abdominal pain in a child should be considered as having relation to the appendix until proved not to have. Particular stress is laid on accurate taking of the history and careful physical examination. Abdominal pain, vomiting, tenderness, rigidity of the right rectus muscle or "muscle guard," "relaxation pain" or "rebound pain" and facial expression and posture are given as reliable guides to accurate diagnosis. Attention is drawn to the fact that children frequently do not localize the pain to the appendical region but often to the umbilicus or to the left side. An excellent list is given of those conditions which may simulate appendicitis in childhood. The warning against use of laxatives and enemas in the presence of abdominal pain is reiterated.

BERKLEY, Los Angeles.

GEE-THAYSEN DISEASE—IDIOPATHIC STEATORRHEA OF ADULTS AND ADOLESCENTS IN NONTROPICAL COUNTRIES. H. MOORE, W. R. O'FARRELL, J. A. GERAGHTY, J. M. HAYDEN and M. A. MORIARTY, Quart. J. Med. **5**:481 (Oct.) 1936.

Moore and his co-workers describe ten cases of idiopathic steatorrhea in adults in detail. The youngest patient was 14 and the oldest 63 years of age. The authors reiterate the opinion of Thaysen that idiopathic steatorrhea of adults in nontropical countries, celiac disease of children and nontropical sprue are all one and the same disease, but they suggest that possibly the etiologic factors may not be quite similar in all three. They suggest that celiac disease in children be designated as the Gee-Herter disease, that idiopathic steatorrhea of adults of nontropical countries be called the Gee-Thaysen disease and that the name "sprue" be retained for the tropical disease.

BRADFORD, Rochester, N. Y.

BANANA THERAPY IN DIARRHEAL DISEASES IN INFANTS AND CHILDREN. C. LORING JOSLIN, South. M. J. **29**:1007, 1936.

Joslin reports on thirty patients with diarrhea who were given the banana therapy. One group was treated with dehydrated banana powder, another with

banana powder to which dextrose and malt extract had been added and a third with raw banana. This treatment appears to prevent loss of weight, and there was in all cases a reduction in the number of stools. SCHLUTZ, Chicago.

IMPAIRED GLUCOSE TOLERANCE IN CERTAIN ALIMENTARY DISORDERS OF CHILDHOOD, WITH REMARKS ON THEIR TREATMENT WITH LIVER EXTRACT. C. W. ROSS, Lancet **2**:556 (Sept. 5) 1936.

Three axioms are stated:

1. The tolerance of any one for dextrose is directly proportional to his sensitivity to injected insulin.

2. Sensitivity to insulin is due to the presence in the body of a third factor in the dextrose-insulin reaction, now usually referred to as insulin kinase.

3. The degree of the sensitivity to insulin and hence of the tolerance to dextrose in a healthy person is determined solely by the amount of carbohydrate which the diet has contained in the period preceding the test.

An association of a flat oral dextrose tolerance curve with a high intravenous one is demonstrated by the author in celiac disease, chronic intestinal indigestion and abdominal glandular tuberculosis. It is believed to indicate a deficiency in the power to absorb carbohydrate from the intestine.

It is also shown that the administration of liver extract either enterally or parenterally improved dextrose tolerance when it was impaired in these conditions.

LANGMANN, New York.

CONCURRENT CHRONIC INTUSSUSCEPTION AND RETROGRADE INTUSSUSCEPTION. J. R. RYAN, M. J. Australia **2**:331 (Sept. 5) 1936.

Ryan reports a case of chronic intussusception in a 7 month old infant. The condition was of six weeks' duration. Although unusual in such cases, blood was passed through the rectum about twenty hours after the first onset and from time to time thereafter. At operation a retrograde intussusception was found in addition to the primary intussusception. Local anesthesia was used, and manual reduction was performed. Recovery ensued. Ryan suggests that the use of enemas in patients who are suspected of having intussusception but in whom no blood has been passed may reveal the presence of blood and thereby be a diagnostic aid.

GONCE, Madison, Wis.

OMENTAL CYST IN A SAMOAN CHILD. G. DEMPSTER, New Zealand M. J. **35**:322 (Oct.) 1936.

A girl of 2½ years with a history of gradual enlargement of the abdomen for eighteen months was found, on exploratory laparotomy, to have a multilocular cyst filled with approximately 5½ quarts (5 liters) of brownish fluid. The cyst formed most of the greater omentum and had its base between the stomach and the spleen in the remains of the gastrosplenic ligament. It was removed, and the child recovered.

MULHERIN, Augusta, Ga.

RAW APPLE TREATMENT OF INFANTILE DIARRHEA. S. F. BAKAL and R. M. SIGAL, Arch. de méd. d. enf. **39**:578 (Sept.) 1936.

Hessing, in 1906, was the first who adopted the raw apple treatment of diarrhea in infancy. Twelve years later the treatment was popularized by Heisler, and in 1930, before the International Congress of Pediatrics at Stockholm, Moro advanced its claim as a specific remedy not only for this disorder but for dyspepsia of various types and for mucous colitis. Only ripe apple reduced to a pulp with a glass grater was recommended, and the amount served varied according to the age of the patient, from 100 to 300 Gm. being administered several

times daily. No other food was offered, but liquids were given sparingly; after the period of so-called "apple days," a mixed diet was employed, consisting of cottage cheese, toast, swiss cheese, finely divided bananas, lean meat, soft boiled egg, puree of potato and tea.

Moro's observations embraced the history of fifty-two patients, nine of whom were nurslings and forty-three children between 1 and 5. In most of these patients the diarrhea was mastered within two days, and there were few relapses. The results were attributed in part to the absorption of toxins in the upper intestine by the partly digested mass, but also to the liberation of annic and malic acids.

Heisler used green fruit, unpared, and also cooked fruit, securing equally good results, which he felt were brought about by the considerable content of malic acid in and immediately beneath the skin of the apple.

Wiscoth, of Munich, recognized the difficulty of administering apple pulp to an infant, and was able to prepare a powder, with 100 Gm. corresponding to 1 Kg. of raw apple. He prescribed from 20 to 24. Gm. of the powder in a 4 per cent solution on the first day of treatment and from 30 to 40 Gm. on the second. In grave cases nothing but tea was given during the first six to twelve hours.

Malyoth gave the apple powder in a decoction of rice and attributed the beneficial effects to the pectin of the apple pulp. Carrot soup, rich in pectin but containing no malic acid, is satisfactory for the treatment of infantile diarrhea but not as efficient as a diet of apple.

Fanconi, of Zurich, advocated the addition of sweet almond milk to the daily ration.

The authors report their observations in a series of fifty-one patients, twenty-eight of these being under 2 years of age, eighteen from 2 to 5 years and five 10 years of age. Bacteriologic investigation in these patients gave entirely negative results. With two of the children, the treatment could not be carried out satisfactorily, but the others took the apple diet eagerly, and the results were uniformly excellent, as shown in the prompt alteration of the number and character of the stools and the notable improvement in the general condition of the patient.

Case histories are cited.

AMESSE, Denver.

GASTRIC AND DUODENAL ULCER IN THE CHILD. I. REYDERMAN, Rev. franç. de pédiat. **11**:608, 1936.

Reyderman reports twelve cases of ulcer in children. He divides these into four groups: In the first group the ulceration had resulted in scarring of the pyloric portion of the stomach, with marked retention and malnutrition. In the second group the condition was of long duration, resulting in malnutrition, and there were the typical symptoms of pain occurring several hours after eating, pain at night and increased gastric acidity, as well as a typical x-ray picture. In the third group the clinical symptoms were similar, but the x-ray findings not as definitely diagnostic. In the last group, composed of five cases, they x-ray picture was apparently normal, but the pain was relieved by food, and hypersecretion in the stomach with high acidity and long duration of the symptoms, with the response to the therapeutic procedure, made the author feel that these, too, were undoubtedly cases of gastric ulcer. He feels that as a rule sufficient weight and consideration are not given to symptoms which may point to gastric or to duodenal ulcer in the child.

LESLIE, Evanston, Ill.

ABDOMINAL PAIN IN CHILDREN: III. GASTRIC SYNDROMES. I. REYDERMAN and A. GUERSTEIN, Rev. franç. de pédiat. **11**:763, 1935.

Two cases of achylia gastrica in which there was an associated infection of the duodenum with Lamblia intestinalis and one case of gastric ulcer in childhood are reported. The authors believe that pathologic alterations in gastric secretions and

gastro-intestinal anatomic lesions are much more common in children than has previously been considered.

They make a plea for better study of the child complaining of abdominal pain.

LESLIE, Evanston, Ill.

HEMORRHAGIC STEATONECROTIC PANCREATITIS WITH HEMOPERITONITIS IN A SYPHILITIC INFANT. G. MACCIOTTA, Clin. pediat. **18**:572 (Sept.) 1936.

After briefly reviewing the literature relating to acute pancreatitis in young children, Macciotta describes the carefully studied case of an infant who had rhinitis, osteochondritis and osteoperiostitis and positive serologic reactions for syphilis (Wassermann, Cantanni, Meineke) in the third week of life. Following treatment with mercury and arsenic, the clinical signs (pseudoparalysis) improved, but an acute illness developed, with cutaneous lesions resembling varicella in the sixth week. Death occurred three days after these lesions developed. At necropsy, in addition to the expected observations, there was bloody peritoneal fluid, apparently originating from the hemorrhagic and necrotic pancreas. Microscopically, the pancreas showed a diffuse inflammatory reaction with supposedly superimposed foci of hemorrhagic fat necrosis. Macciotta speculates as to whether the whole pathologic condition was syphilitic or whether the pancreatitis was a complication of true varicella.

DOOLEY, New York.

INDICATIONS FOR OPERATION IN OBSTRUCTIVE DISTURBANCES OF THE PYLORUS IN INFANCY. E. HAINISS, Arch. f. Kinderh. **108**:130 (June 30) 1936.

The condition of the infant, not the distinction between pyloric stenosis and pylorospasm, should determine the therapy to be used. Operation is indicated (1) when inanition is so severe as to make any delay dangerous, (2) when there is no improvement under conservative treatment and (3) if the symptoms reappear after conservative treatment when the diet is increased sufficiently to permit a normal gain in weight. If the general condition is not too poor, conservative internal treatment should be given a trial.

CRANE, Chicago.

APPENDICITIS IN CHILDHOOD. L. ASCHOFF, Arch. f. Kinderh. **108**:142 (June 30) 1936.

Among cases of true appendicitis in children those in which the pneumococcus is the predominant organism are conspicuous; in other cases the enterococcus is found, as in cases in adults. In children appendicitis frequently results in diffuse peritonitis, while in adults a periappendicular abscess is more common. In many cases of pneumococcic or enterococcic peritonitis in children the polyvalent pneumococcus serum of the mixed enterococcus—colon bacillus—gas bacillus serum of Gundel, injected intraperitoneally, is effective. In addition to true appendicitis, appendicitis due to oxyurids is frequent in children, and also the so-called pseudoappendicitis, which develops without inflammation of the appendix or worm infection.

CRANE, Chicago.

THE OCCURRENCE OF NUMEROUS CASES OF DIARRHEA OF UNCERTAIN ETIOLOGY IN INFANTS. H. BRUGSCH, Arch. f. Kinderh. **108**:177 (June 30) 1936.

An outbreak of severe diarrhea in an infants' home could not be explained except as due to killed colon bacilli or their toxins in the milk. The milk was heated to 90 C. for ten minutes before being used for feeding, so no live organisms could have been responsible, but the untreated milk was found to contain an excessive number of colon bacilli.

CRANE, Chicago.

INFANTILISM AND STUNTED GROWTH IN DUODENALSTENOSIS AND THE DEVELOPMENT OF RICKETS DURING THE INCREASED GROWTH AFTER GASTRO-ENTEROSTOMY. A. BEUTAL and W. NONNENBRUCH, Med. Klin. **32**:765 (June 5) 1936.

This is a carefully detailed report on a boy who had begun to have attacks of vomiting and gastric tetany at the age of 7 years and had then ceased to grow or develop physically. He was brought to a clinic (Deutsches Universität, Prague, Czechoslovakia) at the age of 16 years in an acute attack of severe tetany. His urine was chloride-free; the blood sodium chloride was 0.230 per cent and the nonprotein nitrogen 0.122 per cent. After the administration of saline solution rectally and intravenously and of calcium intravenously, his symptoms ceased; the sodium chloride in the blood rose to 0.427 per cent; the nonprotein nitrogen fell to 0.046 per cent. He weighed 23.4 Kg., was 126 cm. tall and had the general appearance of a child of 7 years. His dentition corresponded to his actual age, but he had pseudo-epiphyses at the proximal ends of both first metacarpals and ossification from only one center in each processus styloideus ulnae. The descending portion of the duodenum could not be visualized roentgenographically because of a huge overlying gastric shadow. On laparotomy, stenosis was found in the region of Vater's papilla, and gastro-enterostomy was performed.

Eight months after operation he was free from symptoms, weighed 37.8 Kg., was 140 cm. in height, showed pubertal changes and normal skeletal development of his wrists but had grown extremely bowlegged and showed roentgen signs of florid rickets. At this time, chemical analyses of the blood gave the following results: whole blood sodium chloride, 0.514 per cent; serum sodium chloride, 0.608 per cent; serum calcium, 9.3 mg. per hundred cubic centimeters; serum potassium, 17.7 mg. per hundred cubic centimeters; serum sodium, 328 mg. per hundred cubic centimeters; alkali reserve, 25.5 volumes per cent; inorganic phosphorus, 4.8 mg. per hundred cubic centimeters; erythrocyte calcium, 4.5 mg. per hundred cubic centimeters; erythrocyte potassium, 4.15 mg. per hundred cubic centimeters; erythrocyte sodium, 98 mg. per hundred cubic centimeters; blood carbon dioxide, 64.4 volumes per cent.

After a month of active antirachitic therapy, the boy showed healing of the rickets and an alkali reserve of 30.3 volumes per cent. DOOLEY, New York.

APPENDICITIS IN EARLY CHILDHOOD. H. LITTNA, Med. Klin. **32**:802 (June 12) 1936.

Among 597 appendectomies performed in the surgical division of the Kinderspital in Prague, Czechoslovakia, within the past year, 7 were in children in the second year of life. Littna sketchily describes these cases without contributing anything new to the general knowledge of his subject. DOOLEY, New York.

RACHITIS HEPATICA. F. THOENES and W. GRUSON, Monatschr. f. Kinderh. **67**:134 (Oct.) 1936.

Thoenes and Gruson report two cases of hepatic disease associated with bony changes typical of rickets. The report includes x-ray pictures of the long bones.

In the first case a nursling of 4 months acquired keratomalacia in spite of excellent feeding. Simultaneously, he showed mild icterus and acholic stools. The diagnosis of atresia of the bile ducts was confirmed at autopsy. With the onset of the symptoms, abundant vitamin A was given by mouth with no benefit. When the vitamin A was given subcutaneously, the rachitic symptoms promptly disappeared. In the second case rickets developed in an infant simultaneously with icterus, diminution in the size of the liver and signs of atresia of the bile ducts and of biliary cirrhosis. In this case the rachitic findings were uninfluenced by any form of vitamin D offered by mouth but were promptly dissipated by treatment with ultraviolet rays. The patient succumbed to the anomaly of the biliary tract.

The writer cites these two cases as clinical evidence against the observations of Gerstenberger. In a report before the German Pediatric Society in 1933, the latter reported cases of a similar condition, which he described as hepatic rickets. He believed that the rickets was due to the disease of the liver. The authors of the present study tend to the belief that hepatic rickets is just the ordinary form of rickets induced by lack of absorption of viamin D from the gastro-intestinal tract.

GERSTLEY, Chicago.

THE ROENTGEN PICTURE OF MECKEL'S DIVERTICULUM. R. PRÉVÔT, Röntgenpraxis **8**:397 (June) 1936.

It is seldom possible to demonstrate Meckel's diverticulum roentgenographically; its occasional visualization is chiefly a matter of chance. A case in point is reported.

MCCUNE, New York.

A CASE OF BILIARY CIRRHOSIS OF THE LIVER DUE TO CONGENITAL BILE DUCT ATRESIA. G. ISHIYAMA, J. Orient. Med. **25**:567 (Sept.) 1936.

The patient was a 50 day old boy, who was brought to Ishiyama's attention because of gradually increasing jaundice. This appeared on the tenth day of postnatal life, with distention of the abdomen, cough and weakness of respiration. The stools were whitish gray; the urine, dark-colored. The temperature was 38 C. (100.4 F.). Examination of the blood showed 3,380,000 erythrocytes, 71 per cent hemoglobin and 18,000 leukocytes, with a normal differential picture; but the bleeding time was twenty-six minutes and the coagulation time twelve minutes. Serologic tests were negative. Postmortem examination established the anatomic diagnosis as follows: congenital absence of the bile ducts and gallbladder, biliary cirrhosis of the liver, pulmonary stenosis, absence of the middle lobe of the right lung, presence of fourteen accessory spleens, hemorrhagic diathesis and bilateral catarrhal pneumonitis of the lower lobes. Fourteen similar instances collected from the literature are reviewed.

KATO, Chicago.

GLYCOGENOSIS (VON GIERKE'S DISEASE): CLINICAL INVESTIGATION OF A CASE OF PATHOLOGIC STORAGE OF GLYCOGEN, TOGETHER WITH A SURVEY OF THE CLINICAL FEATURES OF GLYCOGENOSIS AND OF HEPATIC DWARFISM. A. SUNDAL, Acta pædiat. **19**:80, 1936.

The patient whose case is reported was a white girl whose liver shortly after birth was found to be enlarged. She enjoyed good health during the first eighteen months of life but at twenty-three months suffered a transient attack of jaundice. She did not begin to walk until she was 4 years old; by this time it was apparent that she was destined to be a dwarf. At 10 years she was short and obese; her intelligence was normal. The liver reached to the iliac crest; the spleen could not be felt. The heart was not enlarged. The state of ossification of the skeleton corresponded to that of a 6½ year old child. Among the observations in an extensive chemical investigation, the following are of special interest: The whole blood cholesterol was 275 mg. per hundred cubic centimeters. (The author designates this as hypercholesteremia.) The serum inorganic phosphorus was somewhat decreased. The average of several determinations of the blood sugar in the fasting state was 61 mg. per hundred cubic centimeters; acetone was found in the urine on several occasions, following brief periods of starvation. A diabetic type of dextrose tolerance curve was obtained; acetone disappeared slowly from the urine after the ingestion of dextrose. The blood sugar failed to rise in response to the parenteral injection of 0.75 mg. of epinephrine while the child was fasting; epinephrine increased the excretion of acetone. For fear of producing unpleasant and possibly harmful manifestations of hypoglycemia only 2 international units of insulin was used in order to study the patient's response to this hormone; with this dose the concentration of blood sugar remained unchanged.

Hepatomegaly is the most constant manifestation of glycogenosis; retardation of growth and development is the rule; the skeletal musculature is particularly apt to be weak. Pathologic fragility of the bones has been reported. Moderate anemia may be present. The disease is occasionally familial.

From the chemical point of view hypoglycemia during fasting is an outstanding feature; this seldom manifests itself overtly, although the patients may be conscious of a craving for carbohydrate. Sugar tolerance tests usually result in one or another variant of the diabetic type of blood sugar curve. One of the most characteristic features of glycogenosis is a tendency toward ketosis; acetone appears in the urine soon after the beginning of starvation and disappears only gradually when carbohydrate is given. Patients suffering from von Gierke's disease usually fail to show a rise of blood sugar after injections of epinephrine; this procedure usually increases the excretion of ketone bodies. The patients are peculiarly sensitive to the effect of insulin, and the hormone must be used with considerable caution. The diagnosis of glycogenosis can be confirmed most conveniently by chemical examination of a specimen of liver obtained for biopsy or at autopsy. Pathologic accumulation of glycogen also occurs in the cardiac and skeletal muscles, in the kidneys and in the brain. Some assistance in diagnosis may be obtained from estimation of the concentration of glycogen in the blood. Since the etiology of the disease remains unknown, it is not possible to delimit the condition sharply from other pathologic states characterized by hepatomegaly, dwarfism and anomalies of the metabolism of carbohydrate. A logical method of treatment has not yet been proposed.

The paper supplies a good bibliography. McCUNE, New York.

INTESTINAL INFANTILISM AND PSEUDOPERNICIOUS ANEMIA. W. K. DICKE, Maandschr. v. kindergeneesk. **5**:406 (July) 1936.

Dicke reports a case of pseudopernicious anemia in Herter's disease; the anemia was cured only by intravenous injections of a strong preparation of liver. Though the symptoms of Herter's disease still existed at the time of writing, the child had remained in good condition without further injections of liver for nearly two years. VAN CREVELD, Amsterdam, Netherlands.

A PECULIAR CASE OF ILEUS IN A NEW-BORN INFANT. J. VAN DER SPEK, Nederl. tijdschr. v. geneesk. **80**:3468 (July 25) 1936.

Van der Spek reports a case of hernia of the intestinal wall (described for the first time in 1778 by Richter) in an infant of 8 weeks, with quick recovery after the operation. VAN CREVELD, Amsterdam, Netherlands.

## Nervous Diseases

PETIT MAL IN CHILDREN. R. C. HAMILL, Am. J. Psychiat. **93**:303 (Sept.) 1936.

Some sixty epileptic children were studied whose attacks of petit mal ranged widely in severity and number. In every case the sensations were described as lying somewhere between the lips and the pylorus. Among boys, particularly, there seems to be a definite relationship between temper tantrums and epilepsy. Cases are described in which therapy based on the psychogenetic principles underlying petit mal seizures met with a fair degree of success. JAHR, Omaha.

MULTIPLE TELANGIECTASES OF THE BRAIN: A DISCUSSION OF HEREDITARY FACTORS IN THEIR DEVELOPMENT. J. C. MICHAEL and P. M. LEVIN, Arch. Neurol. & Psychiat. **36**:514 (Sept.) 1936.

Five members of a family suffered from convulsive seizures with focal manifestations. Multiple areas of calcification of the brain were demonstrable in the x-ray plates of the heads of two of the children. Pathologic examination of the brain of one of these children showed the calcified tissues to be telangiectases of the brain.

Michael and Levin describe other cases and discuss the subject in general. In one case, the symptoms resembled pontile tumor. The history varied from the usual history of tumor, however, by the presence of intermittent coma. The disease is apparently hereditary. The observation of multiple areas of certification of the brain in the x-ray plate is of great value in diagnosis.

BEVERLY, Chicago.

CEREBRAL FRONTAL AGENESIS IN ASSOCIATION WITH EPILEPSY. J. F. BATEMAN, Arch. Neurol. & Psychiat. **36**:578 (Sept.) 1936.

Bateman reviewed the clinical and pathologic data on the brains of 108 persons coming to autopsy in a state hospital who had suffered from convulsions and had neurologic findings. In 66 cases the onset occurred before the patient was 12 years of age. In 60 of the patients the frontal lobes showed atrophy. In those in whom convulsions developed after pubescence, the incidence of atrophy was no greater than in a series of persons with psychoses whose brains were used as controls. For this and other reasons, Bateman feels that the atrophy occurring before pubescence is due to cerebral frontal agenesis. Atrophy or agenesis alone does not explain convulsions. If it did, they would be continuous.

BEVERLY, Chicago.

THE CALCIUM CONTENT OF THE BLOOD SERUM DURING AN EPILEPTIC CONVULSION. M. SCOTT and A. W. PIGOTT, Arch. Neurol. & Psychiat. **36**:590 (Sept.) 1936.

The calcium content of the blood serum during an epileptiform convulsion is not appreciably different from that determined in the same patient between seizures. Hypocalcemia is uncommon in patients with epilepsy.

BEVERLY, Chicago.

THE SHOULDER SIGN. S. M. WEINGROW, Arch. Pediat. **53**:413 (June) 1936.

Weingrow describes a scapular tendon reflex which is of value as a sign of pyramidal tract disease. The reflex is elicited by having the patient place the arm, forearm and hand in their normal position, preferably at rest with the hand in the patient's lap. Tapping the acromial portion of the scapula or the coracoid process produces slight flexion of the forearm and slight internal rotation of the hand. He has elicited this reflex occasionally in normal persons.

ORR, Buffalo.

MYELOMALACIA IN A THREE YEAR OLD CHILD. HARRY A. SPIGEL, Arch. Pediat. **53**:500 (July) 1936.

Spigel reports a case of myelomalacia occurring in a 3 year old Negro girl. The onset of the disease was insidious, with vague pains in the back and the right knee joint, gradually changing to limping and finally to paralysis, first of the lower extremities and later of the upper extremities and the back, extending to the sphincters of micturition and defecation, finally involving the muscles of respiration and deglutition.

Microscopic examination of the spinal cord showed areas of degeneration with cavitation involving the gray matter. The greatest involvement occurred in one anterior horn and extended throughout the thoracic portion of the cord. The other horns of gray matter were involved to a lesser degree. Small areas of similar nature were found in other levels of the cord. These areas were poorly defined and surrounded by varying amounts of degenerated tissue. The changes were not typical of syringomyelia, nor was the perivascular infiltration of poliomyelitis noted.

In most cases myelomalacia is the result of spinal trauma. Spigel considers that sepsis was a possible etiologic factor in his case, because of the presence of a purpuric eruption and low grade fever.

ORR, Buffalo.

ARTIFICIAL FEVER TREATMENT OF CHOREA. C. H. BARNACLE, J. R. EWALT and F. G. EBAUGH, J. A. M. A. **106**:2046 (June 13) 1936.

Thirteen patients with chorea minor of moderate or severe type were treated with the Kettering hypotherm. The results have been gratifying, with recovery in all and no recurrences in the short period of observation. Advanced rheumatic endocarditis has been no contraindication to this treatment. Mechanically induced fever has an advantage over fever produced by triple typhoid vaccine, namely, avoidance of chills, vomiting, headache, prostration and shock.

BONAR, Salt Lake City.

TREATMENT OF CHOREA MINOR BY MEANS OF ELECTROPYREXIA. C. A. NEYMANN, M. L. BLATT and S. L. OSBORNE, J. A. M. A. **107**:938 (Sept. 19) 1936.

Artificial fever was produced by electromagnetic induction in twenty-five patients with chorea minor. On the average four treatments were given each patient. The average period of treatment and hospitalization was sixteen days. In all the patients the choreiform movements ceased promptly. In three children there were recurrences. Electropyrexia is not contraindicated when carditis accompanies chorea. This method of producing hyperpyrexia seems superior to methods dependent on external heat.

BONAR, Salt Lake City.

STATUS PIGMENTATUS: ITS PATHOLOGY AND ITS RELATION TO HALLERVORDEN-SPATZ DISEASE. MAX HELFAND, J. Nerv. & Ment. Dis. **81**:662 (June) 1935.

At the age of 11 years, the patient, who until that time had been a healthy girl with a normal developmental and family history, began to complain of swelling of the feet and needle-like pains in the legs. These symptoms persisted, and the family was advised by a physician that there was "something wrong" with the spinal cord. At the age of 16 when she was examined in the clinic, she had pes equinus, hammer toes, limitation of movement of the joints and slight kyphosis of the upper part of the spine. The papillae were pale, especially in the right eye, and were most marked in the temporal half of the disk. Active motility was limited in the lower extremity, with resistance to passive motion, loss of the lower right superficial abdominal reflex, increase in deep reflexes and no clonus but a positive Babinski sign on each side. She showed intention tremor of the left lower extremity and walked slowly and on a broad base.

The behavior changed progressively, and peculiar mannerisms developed. Gradually the mentality declined, and in a few years the patient became utterly infantile in behavior, helpless, silly, bedridden, crying, shouting and laughing spontaneously. With incontinence of the urine and feces, decubitus set in, and she died at the age of 25.

The autopsy showed increased pigment and an increased reaction to tests for iron in the globus pallidus and the zona rubra, scarcity of pigment in the substantia nigra, locus caeruleus and ala cinera, absence of iron in the dentate nucleus, loss of ganglion cells in the corpus striatum, characteristic balloon cells of Pick's disease, swelling of the axis-cylinders in various points of the brain, increase of glia cells in the striatum and cortex and disturbance of fat distribution.

Discussing the clinical picture and the pathologist's report of this case, the author concludes that this disease is an anatomic syndrome characterized by a metabolic disturbance consisting of a distortion of pigmentation in the central nervous system, occurring especially in the centers of the extrapyramidal system. He suggests status pigmentatus as a descriptive synonym for this pathologic syndrome, which may occur as a primary ailment but which may also be observed as a secondary accompaniment to other diseases.

JAHR, Omaha.

THE BLOOD-SUGAR IN CONVULSIONS OF INFANCY AND CHILDHOOD. M. B. MACLEAN, Arch. Dis. Childhood **11**:247 (Oct.) 1936.

The blood sugar content was estimated at frequent intervals after a convulsion in fifty children. It was found that when the first estimation was made sufficiently soon after a convulsion, there was hyperglycemia in nearly half of the cases. In half the cases hypoglycemia occurred some hours after the convulsion and persisted in spite of taking food. In two cases administration of epinephrine during the hypoglycemic phase was followed by a significant rise of the blood sugar level. Except in cases of true hyperinsulinism, it appears that hypoglycemia plays no part in the causation of convulsions in childhood and that the upset in the carbohydrate metabolism is the result and not the cause of the convulsion.

KELLY, Milwaukee.

AGE INCIDENCE OF EPILEPSY. A. J. M. BUTTER, Brit. M. J. **2**:714 (Oct. 10) 1936.

Butter contributes an analysis of admissions to epileptic colonies, showing at what age epilepsy usually begins. One interesting fact is that in only 6 per cent of the cases had epilepsy developed before the age of 5 years.

ROYSTER, University, Va.

SUBARACHNOID HAEMORRHAGE (? OF TRAUMATIC ORIGIN). D. PATERSON, Proc. Roy. Soc. Med. **29**:1435 (Sept.) 1936.

A boy of 7 years was admitted to the hospital because three days before admission he had a sudden pain in the left side of the head. He soon became drowsy and had occasional delirium. Four weeks before this he had fallen and struck his head against a chair. He was stunned at the time but did not lose consciousness. A lump appeared on the left side of the head but disappeared in a few days. A week later mumps developed. From this he recovered and returned to school.

On examination the child was confused. No abnormal signs were found in the nervous system. The optic fundi were normal.

The investigations are given in detail.

WILLIAMSON, New Orleans.

THE TONIC REACTIONS OF THE NORMAL CHILD DUE TO POSITION AND MOVEMENT. R. MESINA, Riv. di clin. pediat. **34**:510 (June) 1936.

The tonic reactions resulting from position and movement were observed in 150 normal children. Especial attention was paid to the time of their appearance and disappearance.

When something, such as a finger, is put into the mouth of a child, the child will press on it with his lips. This reaction is present in all normal babies at birth. At the end of one year it is present in 57 per cent of babies and at the end of a year and a half in but 7 per cent.

When something is placed against the palm of a baby's hand, the baby will grasp it strongly. This grasping reaction is present in all babies at birth, in 90 per cent of babies in the first six months of life, in 69 per cent in the second six months of life and in 33 per cent in the third six months of life.

A similar grasping reaction of the feet is noticed when the finger is pressed along the sole near the toes. At birth all babies show this reaction. It is present in 96 per cent of babies in the first six months of life, in 71 per cent in the second six months of life and in 40 per cent in the third six months of life.

If when a baby lies on its back one leg is taken and flexed, the other one will be drawn automatically into the same position. This reaction is present in all babies up to 3 months of age. During the second six months of life it is found in 76 per cent of babies, and in the third six months of life, in only 27 per cent.

If a baby is held face down and slowly elevated, the child may show extension of the head, a tendency to opisthotonos and flexion at the elbow and at the knee.

This phenomenon appears in children at about 2 months of age. It is present in 96 per cent of children between 3 and 6 months of age and in only 61 per cent in the second half year of life. A similar reaction may be observed in children held suspended by their feet.

Other reactions of the neck and of the eyes are described, as are the reactions to standing and crawling.

HIGGINS, Boston.

EPILEPSY AND HEREDITARY SYPHILIS. M. SAMAIA, Riv. di clin. pediat. **34**:532 (June) 1936.

Samaia reports the case of a boy 10 years of age with convulsions over a period of fourteen months. The convulsions occurred at intervals of a few days to two months. On physical examination nothing abnormal was detected except a diminished tendon reflex on the left. The spleen was not palpable. The Wassermann reaction of the blood was negative, but that of the spinal fluid was strongly positive. The spinal fluid showed 1 lymphocyte. The Pandy test was negative. The parents were shown by clinical examination and the Wassermann test to be normal, although the mother had had several abortions. Treatment of the boy with neoarsphenamine changed the character of the attacks from the grand mal type to rare clonic movements of the facial muscles at infrequent intervals and without loss of consciousness.

HIGGINS, Boston.

THE METABOLISM AND IMPORTANCE OF IODINE IN CHILDREN: II. THE IODINE CONTENT OF THE CEREBROSPINAL FLUID IN CHILDREN FROM BIRTH TO NINE YEARS. G. CONCAS, Riv. di clin. pediat. **34**:882 (Oct.) 1936.

Concas has made observations on the content of iodine in the cerebrospinal fluid and in the blood of forty-nine children. In all but three of the children the content in the blood was greater than that in the spinal fluid. It is impossible to set a definite value for the iodine in the cerebrospinal fluid, as the results of analyses vary by reason of differences in age, sex, food, activity and meningeal permeability toward iodine.

HIGGINS, Boston.

KORSAKOFF'S SYNDROME IN A CASE OF TUBERCULOSIS. J. SOBRINHO GONCALVES, J. de pediat., Rio de Janeiro **3**:454 (Oct.) 1936.

Korsakoff's syndrome of confusion, with mental agitation, hallucinations and amnesia, was observed in a boy of 9 years. Associated with this were loss of weight and loss of tendon reflexes. Skin tests with tuberculin were negative. The boy died with gastro-intestinal symptoms. Autopsy revealed a pulmonary focus of tuberculous infection and disseminated intestinal involvement. This is an unusual case because of the sex and because of the fact that tuberculosis is not as a rule an exciting factor in this syndrome.

SANFORD, Chicago.

HYDROCEPHALUS WITH SPINA BIFIDA. VICTOR DO AMARAL FILHO, Rev. de gynec. e d'obst. **29**:24 (Jan.) 1935.

Do Amaral Filho reports a single case of hydrocephalus following spina bifida.

HERRON, Spokane, Wash.

TUMORS OF THE BRAIN IN THE FIRST TEN YEARS OF LIFE. H. DI GASPERO, Arch. f. Kinderh. **108**:149 (June 30) 1936.

This article is a survey of the clinical picture, course, pathologic anatomy and histopathology of tumors of the brain in children under 10 as compared with those found in older persons.

CRANE, Chicago.

HISTOPATHOLOGIC CHANGES IN THE CENTRAL NERVOUS SYSTEM IN EXPERIMENTAL EXSICCOSIS AND TOXICOSIS. S. J. SCHAFERSTEIN, N. A. POPOWA and E. P. OWTSCHARENKO, Jahrb. f. Kinderh. **145**:210 (Oct.) 1935.

Exsiccosis or toxicosis was produced in young dogs by three measures, namely, high temperature of the surroundings, concentrated diet and artificially induced diarrhea. The protocols of various animals are given. The central nervous system was studied, and the pathologic changes are described in detail.

LANDAU, Hannibal, Mo.

THE DIAGNOSTIC IMPORTANCE OF INFECTIOUS ENCEPHALOMENINGITIS IN RELATION TO TUBERCULOUS MENINGITIS AND POLIOMYELITIS. O. GÖBELL and W. KELLER, Kinderärztl. Praxis **7**:216 (May); 258 (June) 1936.

The authors report four cases of what Wallgren was the first to describe as acute aseptic meningitis. The cases occurred within eleven days. The authors believe that the name given by Wallgren is misleading, because the occurrence of the disease in small epidemics has also been observed by others and because the disease has been transferred by Eckstein to monkeys, facts both of which speak against the use of the term "aseptic." Further experience has shown that there are many cases of so-called acute aseptic meningitis in which, besides all the symptoms of meningitis, the patients show encephalitic symptoms, also, as, for instance, paresis of the ocular muscles. The authors consequently prefer to use the term "infectious encephalomeningitis" or "encephalomyelomeningitis" and to consider that the disease is due to a virus.

As the onset may be subacute and is frequently observed in the spring, differentiation from tuberculous meningitis may be extremely difficult. A positive reaction to tuberculin, the presence of tubercle bacilli in the spinal fluid and a diminished content of sugar in the spinal fluid are diagnostic aids. A normal or even a high content of sugar in the spinal fluid should always cast doubt on the diagnosis of tuberculous meningitis.

Differentiation between encephalomyelomeningitis and poliomyelitis in the preparalytic stage may be impossible, unless paresis typical of poliomyelitis appears. The findings in the spinal fluid may be identical in both conditions, and the content of sugar in the spinal fluid is normal or high normal in poliomyelitis as well as in encephalomeningitis. The authors believe that neither the virus of poliomyelitis nor the meningococcus has etiologic significance for infectious encephalomeningitis.

HEYMANN, Cleveland.

COMPARATIVE STUDIES OF THE REDUCING SUBSTANCE PRESENT IN THE VENTRICULAR AND SPINAL FLUID OF HYDROCEPHALIC CHILDREN. S. AHNSJÖ, Acta pædiat. **19**:141, 1936.

In a carefully conducted piece of work Ahnsjö found no difference in concentration of reducing substance between the cerebrospinal fluid obtained from the cerebral ventricles and that withdrawn simultaneously from the lumbar subarachnoid space. The blood sugar rose considerably during the brief time required to withdraw the spinal fluid. However, samples of fluid taken between seven and eighteen minutes after the first specimens did not show an increase in the concentration of reducing substance; the concentrations of sugar in ventricular and lumbar fluid remained equal. Three patients with congenital hydrocephalus of the communicating variety served as the subjects. Similar studies were made in a case of transitory staphylococcic meningitis. The results were in agreement with the aforementioned results except in one instance, which is discussed in detail.

MCCUNE, New York.

## Psychology and Psychiatry

CONTROL OF BEHAVIOR: ITS MECHANISM AND EVOLUTION. C. J. HERRICK, Am. J. Psychiat. **93**:249 (Sept.) 1936.

This is a philosophic discussion of comparative psychology and of the principles governing behavior in man.

JAHR, Omaha.

ORGANOTHERAPY IN MENTAL RETARDATION ASSOCIATED WITH ENDOCRINE AND NON-ENDOCRINE CONDITIONS. M. B. GORDON, L. KUSKIN and J. AVIN, Endocrinology **19**:572 (Sept.-Oct.) 1935.

In this paper Gordon and his co-workers report the effects of treating children suffering from mental retardation by organotherapy. They limited the study to 317 mentally retarded children, who were under observation for at least one year. Signs and symptoms of endocrine dyscrasia were present in 155 children and manifestations of mental retardation of nonendocrine origin in 162. The organotherapy consisted in the administration of desiccated thyroid and pituitary substance in various doses and combinations. Thyroid gland was given by mouth in an initial dosage of 1/10 grain (0.006 Gm.) twice a day for the first week and three times a day for the third week. No medication was given during the second and fourth weeks. This alteration was adhered to with an increase in dosage every month to 1/8, 1/4, 1/2 and 1 grain (0.008, 0.016, 0.032 and 0.065 Gm.). When the 1 grain dose was reached, the therapy was discontinued for the fourth week. In some instances thyroid was given twice a day for the first week of each month and three times a day for the second and third weeks. In a few instances the maximum dosage was increased to 2 grains (0.13 Gm.) three times a day. The authors have found in the past twenty years that this cautious method of treatment affords an adequate check on intolerance and overdosage. In former years whole pituitary substance was administered by mouth, but this has been changed in the past five years to desiccated anterior lobe of the pituitary gland as a better standardized product. The initial dose of the latter is 1 grain three times a day, which is increased every month by 3 grains (0.19 Gm.) a day until 5 grains (0.32 Gm.) three times a day is reached. The pituitary preparation is given three times a day for the first three weeks of each month and then discontinued for the fourth week.

In children with adiposogenital dystrophy, thyropituitary obesity or hypogonadism, extract of the anterior lobe of the pituitary gland or the gonadotropic hormone from the urine of pregnant women is given by hypodermic injection, 1 cc. twice a week. In addition to organotherapy, remedial measures were attempted to eliminate malnutrition, focal infections, orthopedic conditions, defective vision, disturbances of hearing and speech, carious teeth and constitutional diseases, such as syphilis, tuberculosis and rickets. Diets were generously supplied with vitamins, minerals and proteins. Educational measures were undertaken in muscular coordination, sense training and academic study. Social conditions were studied by several agencies, and attempts were made to remedy faulty situations by cooperative efforts of school authorities and social and medical agencies.

In an evaluation of the therapeutic value of each of these measures, the authors believe that diet, improvement in social conditions and elimination of physical disabilities had no effect on the mental status in any child in the series. The change in mentality is due, they believe, to organotherapy or to the educational measures. The part played by the latter is great, but since practically all of the children of school age, especially those of lower mentality, had the benefit of a more or less standardized educational program, it must be concluded that any beneficial results are to be attributed to the effects of glandular preparations. The results obtained were: A tendency to continued improvement was observed in 45 per cent of the group with endocrine disorders and in 1.2 per cent of the group in which mental retardation was not associated with endocrine disturbance.

In the former group fair or temporary results were obtained in 34 per cent and poor results in 21 per cent, while in the latter group fair or temporary results were obtained in 34.6 per cent and poor results in 64.2 per cent. A tendency to continued improvement following the administration of desiccated thyroid and pituitary gland was noted only in cases of mental retardation which were associated with endocrine disorders. The highest incidence was noted in cases of deficiency of the anterior lobe of the pituitary gland, childhood myxedema, hypothyroidism and pituitary obesity, in the order named. Better results (58 per cent) were obtained in the children with thyroid disturbances than in those with hypopituitarism (30 per cent). According to the experience of the authors, the administration of desiccated thyroid and pituitary glands will neither cure nor tend to produce a continuous improvement in mental retardation associated with nonendocrine conditions. The most that can be expected are fair or temporary results. It is concluded that in the treatment of associated endocrine and nonendocrine disturbances, organotherapy can be expected to produce an improvement in endocrine symptoms but not in mental retardation or in the nonendocrine condition.

PALMER, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

THE CONCEPT OF MENTAL DEFICIENCY IN THEORY AND PRACTICE. DAVID WECHSLER, Psychiatric Quart. **9**:232 (April) 1935.

Mental deficiency, involving not only a lack of intellectual skill but an incapacity to apply intelligence to life situations, cannot be defined entirely in terms of an intelligence quotient, since the psychometric test at its best measures intellectual efficiency only and not really ability to apply intelligence. A case is cited in which a young man with an intelligence quotient of 91 had presented a persistent moral problem, was repeatedly antisocial and was apparently chronically unable to meet the ordinary requirements of adjustment to social life. This is contrasted with the case of a native rural laborer with a mental age of 8 who made a good living, supported a family and was for all practical purposes a good, useful citizen. At least three types of mental deficiency must be defined: (1) emotional or moral deficiency, (2) social or vocational deficiency and (3) intellectual deficiency in the narrow sense of the phrase.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

## Diseases of the Genito-Urinary Tract

CONGENITAL PORPHYRINURIA—A POSTSCRIPT. A. GARROD, Quart. J. Med. **5**:473 (Oct.) 1936.

Garrod describes the present status in three cases of congenital porphyrinuria previously reported by Ashby (*Quart. J. Med.* **19**:375, 1925-1926). When the cases were described in 1926, the ages of the patients were 9, 4, and 18 years, respectively. This account of a ten year follow-up in cases of this rare condition should be of considerable interest to those particularly interested in the metabolism of pigment.

BRADFORD, Rochester, N. Y.

TREATMENT OF NEPHROSIS. R. PLATT, Brit. M. J. **2**:548 (Sept. 12) 1936.

The study is introduced by a general discussion. Then follows a consideration of general management. Dietetic treatment is next taken up, with emphasis on the use of protein. Platt suggests the following diet, which he thinks fulfils the requirements for treatment by restriction of salt and water with liberal supply of protein and minimal use of fat.

Breakfast: 5 ounces (141.7 cc.) of tea or coffee with skimmed milk; 4 ounces (113.5 cc.) of fish; bread; marmalade.

Midmorning meal: One small orange or apple.

Lunch: Oysters if procurable; 4 ounces of lean meat or chicken; peas, beans or lentils; milk pudding; 3 ounces (85 cc.) of fluid.

Tea: 5 ounces of tea with skimmed milk; 2 ounces (57 cc.) of fish or lean meat; 6 ounces (170 cc.) of salad or fruit.

Supper: 4 ounces of fish or lean meat; vegetables, salad or mushrooms; 5 ounces of tea or coffee with skimmed milk.

No salt is to be cooked or eaten with the food. No extra fluid is to be used. The fluid allowance should be restricted in proportion to the average weight for age, the actual weight being unreliable on account of edema.

*Treatment with Drugs.*—Since there is no specific treatment, Platt feels that treatment by means of drugs should consist of a further attack on the edema. Urea, he feels, is usually sufficient. In obstinate cases mercurial diuretics may be tried, but only when the essential criteria of diagnosis have been fulfilled, i. e., absence of hematuria, high blood pressure or nitrogen retention. Drugs of this group act more efficiently if the patient has received, some days beforehand, one of the acid-producing salts. For this purpose he prescribes ammonium chloride in extract of glycyrrhiza. Iron should be prescribed if anemia is present. Thyroid extract or thyroxin is extremely well tolerated. Platt thinks these improve the general condition and encourage diuresis. Constipation should be avoided.

*Mechanical Treatment of Edema.*—If the pleural cavities are involved, the fluid should be removed. Ascites should be tapped only if the discomfort is marked. Subcutaneous edema should not be relieved by incision except occasionally edema of the genitals when it is difficult for the patient to void. Sweating is of value at times.

*Treatment of Infections.*—Infections should be prevented as far as possible and treated appropriately when they arise.

ROYSTER, University, Va.

DISCUSSION ON ENURESIS. Proc. Roy. Soc. Med. **29**:1515 (Sept.) 1936.

Miss Robina S. Addis, speaking for Dr. W. Moodie, stated that no satisfactory cure has yet been discovered for the common troublesome symptom of enuresis. It does not appear to be an entity. It does not occur only in the timid or in the aggressive child. It occurs in all types, in all classes and environments and after every variety of training.

A statistical survey was made of all new patients admitted to six of the Child Guidance Clinics in London. The enuretic children were picked out and compared with the remaining nonenuretic children as to incidence, intelligence quotients and ages.

Under the heading of intensive work Miss Addis discussed the selection of cases, method used, cures obtained, nocturnal and diurnal enuresis, onset, routine management, habit training, homes from which the patients came, health, school life and pedigrees of the children.

Dr. Reginald Miller then discussed enuresis from the pediatric point of view, and Dr. W. D. Winnicott took up the subject from the psychiatric side.

WILLIAMSON, New Orleans.

PYELITIS IN INFANTS AND YOUNG CHILDREN. S. MEKLER, Arch. de méd. d. enf. **39**:585 (Sept.) 1936.

Relatively speaking, pyelitis cannot be considered a common disorder of very young children, yet its occurrence in such subjects, even in nurslings of a few months, is obviously less rare than is believed.

Unless urine, especially that of female infants, is examined as a routine procedure, the diagnosis may not be made.

An extended discussion of primary and secondary pyelitis, with the current views concerning the etiologic factors involved, particularly in colibacillemia, is followed by a brief review of the more recent methods of treatment.

AMESSE, Denver.

CATATONIA DUE TO PYELITIS. L. RIBADEAU-DUMAS and others, Nourrisson **24:** 268 (Sept.) 1936.

This report concerns a baby girl, aged 5 months, who was sent into the Salpêtrière, Paris, with a diagnosis of meningitis, which the examination of the spinal fluid did not confirm. Further search disclosed pyuria, which was thought to be the cause of the fever and the unusual neurologic symptoms, prominent among which was catatonia. The rôle of a neurotropic toxin of the colon bacillus is discussed.

McCLELLAND, Cleveland.

INVESTIGATIONS OF BLOOD IN A CASE OF LEVULOSURIA. K. OSTER, Monatschr. f. Kinderh. **67:**155 (Oct.) 1936.

Oster adds one more case to the few reported of levulosuria. This symptom was observed in a 7 year old girl. She had been in good health, and the finding of sugar in the urine was an accident. She had no signs of diabetes, such as polydipsia, polyuria or pruritus. When she ate a diet rich in fruit, sugar was found in the urine. Various tests showed this to be levulose. Adding 100 Gm. of dextrose to a levulose-free diet caused no glycosuria. Adding 10 Gm. of levulose led to excretion of 8.6 per cent of the levulose.

Giving the child 2 Gm. of dextrose per kilogram of body weight and the same amount again in three hours did not lead to glycosuria. The blood sugar did show a slight delay in returning to normal after each of these experiments. When the same amount of levulose was given, the same results were obtained except that the blood sugar curve rose a little higher and fell a little more precipitately. When 20 Gm. of levulose was given in one dose, there was an increase of 48 mg. per hundred cubic centimeters, which sank back to zero after three hours.

GERSTLEY, Chicago.

EXTERNAL MASCULINE PSEUDOHERMAPHRODITISM. G. B. LAUWERS, Nederl. tijdschr. v. geneesk. **80:**4186 (Sept. 19) 1936.

A case of this condition in a girl of 21 years is described. Lauwers discusses the line of treatment to be followed in such a case.

VAN CREVELD, Amsterdam, Netherlands.

## Diseases of the Ductless Glands; Endocrinology

CEREBRAL LESIONS IN UNCOMPLICATED FATAL DIABETIC ACIDOSIS. E. S. DILLON, H. E. RIGGS and W. W. DYER, Am. J. M. Sc. **192:** 360 (Sept.) 1936.

The clinical and chemical findings in eight fatal uncomplicated cases of diabeitc acidosis are described, and descriptions of the cerebral lesions are given. There is cerebral anoxia, primarily based on reduced volume of blood with hemoconcentration. As a result of the reduction in the volume of blood there is marked reduction in the pressure, both systolic and diastolic. This causes reduction in the cerebral blood flow since, as has been shown, cerebral blood flow passively follows changes in blood pressure. Owing to the absence of a vasoconstrictor mechanism in the intracerebral vascular bed, stasis occurs more rapidly in the brain than in other portions of the body and leads to local anoxia of the capillary wall. This anoxia is further increased by the inability of concentrated blood to take up oxygen as readily as normal blood. Owing to these factors there is an increase in the permeability of the capillary wall. The increased permeability occasions cerebral edema. Once the edema is established, rapid death of the cells takes place because of their intolerance of stagnant tissue fluids and their high oxygen requirements.

HENSKE, Omaha.

ARTERIOSCLEROSIS IN YOUNG DIABETICS: A METHOD FOR ITS RECOGNITION BY ARTERIAL ELASTICITY MEASUREMENTS. P. HALLOCK, Am. J. M. Sc. **192:**371 (Sept.) 1936.

The diabetic state either initiates early or accelerates premature arteriosclerosis in the young adult.

The velocity of the pulse wave was utilized in studying arterial elasticity in the large and medium-sized arteries of twenty-two young diabetic patients. To test the significance of the pulse wave velocities obtained in this study the well known chi-square test was employed.

HENSKE, Omaha.

EFFECT OF COMPLETE RENAL INSUFFICIENCY ON THE ACTION OF PARATHYROID HORMONE IN THE DOG. W. R. TWEEDY, R. D. TEMPLETON and F. A. MCJUNKIN, Am. J. Physiol. **115**:514 (May) 1936.

Complete renal insufficiency was induced in dogs by bilateral nephrectomy or by ligation of the renal arteries and veins. Injection of parathyroid hormone following the operative procedure did not produce marked increase in the serum calcium. The increase in serum inorganic phosphorus was not retarded. The authors observed no gross signs of an overdosage of the hormone, such as venous engorgement and hemorrhage in the stomach, indicating that the complete deletion of renal function protected the animals from the effects of an overdosage of parathyroid hormone. Their results form the view that the kidney plays a dominant rôle in the action of the parathyroid hormone.

NOURSE, Cleveland.

EFFECT OF OVARIAN HORMONE ON THE BASAL METABOLISM OF EXPERIMENTAL HYPERTHYROID RATS. T. C. SHERWOOD and LINWOOD M. BOWERS, Am. J. Physiol. **115**:645 (May) 1936.

The experiments reported indicate an influence of the ovarian over the thyroid function in the control of the basal metabolism. Injections of an estrogenic substance produced a return of the basal metabolism to normal in less than half the usual time.

NOURSE, Cleveland.

EFFECTS OF THE ORAL ADMINISTRATION OF PITUITARY EXTRACT. L. LURIE, Arch. Pediat. **53**:379 (June) 1936.

Two patients with dystrophia adiposogenitalis were treated successfully by oral administration of an extract of whole pituitary gland. The dosage in each case was 6 grains (0.388 Gm.) daily. In both cases there was no restriction of diet.

The first case was that of a white boy of 15 years who was 49½ pounds (22.4 Kg.) overweight for his height and age and presented the typical findings of dystrophia adiposogenitalis. He was under treatment for six months and lost 39 pounds (17.7 Kg.) in weight. Secondary sex characteristics gradually developed.

The second case was that of a white boy of 12 years who was 90 pounds (40.8 Kg). overweight for his height and age and presented a distinctly feminine appearance. In this instance two years elapsed before treatment was started. During that time he gained 38 pounds (17.2 Kg.). Treatment was carried on over a period of one year. He lost 58 pounds (26.3 Kg.), and secondary sex characteristics developed. Excellent photographs illustrate the results obtained.

Lurie does not agree with the widespread opinion that whole pituitary gland is ineffective when administered orally. He contends that successful results are dependent on the case of a potent preparation and the proper selection of cases.

ORR, Buffalo.

POLYURIA AND POLYDIPSIA (DIABETES INSIPIDUS) AND GLYCOSURIA RESULTING FROM ANIMAL EXPERIMENTS ON THE HYPOPHYSIS AND ITS ENVIRONS. F. L. REICHERT and W. E. DANDY, Bull. Johns Hopkins Hosp. **58**:418 (June) 1936.

"Since polyuria and polydipsia follow injuries to the hypothalamus after the hypophysis has been removed, the conclusion is inescapable that diabetes insipidus is not due to the absence of a hypophyseal hormone. Since the paraventricular

and supra-optic nuclei have unquestionably been traumatized by our mechanical and thermal injuries to the hypothalamus and with no greater effect than without such injury, we cannot believe that the center of water control is represented by these nuclei. It is our belief that only the human experiments will solve this problem.

". . . the incidence and degree of glycosuria are essentially the same in the control animals in which no attack was made upon the hypophysis or upon the base of the brain as when various operative procedures were carried on these structures. Always the urinary sugar is transient and usually it occurs only in the first specimen; occasionally it persists for 24 to 48 hours. Even in dogs without anaesthesia or medication of any kind, glycosuria will be demonstrable at times. In another somewhat larger series of dogs not included in this report, glycosuria was found in four. From these observations we see no reason to infer that the hypophysis, the hypothalamus, or any part of the base of the brain in this region, has any particular bearing on the production of glycosuria in dogs."

AUTHORS' SUMMARY.

THE SUBTHYROID CHILD. E. J. LAMB, California & West. Med. **44**:371, 1936.

Lamb presents certain symptoms and signs together with laboratory findings which point to a diagnosis of hypothyroidism at an early age. In the history one should consider the stature, evidences of allergy and endocrinopathy among members of the immediate family, amount of overweight or underweight since birth and abnormalities of weight and of growth increment, together with evidences of retarded development, both physical and mental. Allergic manifestations often point to hypothyroid tendencies. Indicative of hypothyroidism are: underweight and underheight, overweight and underheight or underweight and overheight, together with dry, eczematous skin; abnormalities of the teeth, including caries and malocclusion; slow pulse and subnormal temperature; infantile genitalia; protuberant abdomen, and flat feet. Laboratory data should include studies of the bone age, together with visualization of the sella turcica by x-rays, since pituitary imbalance should always be considered in connection with suspected thyroid imbalance; sugar tolerance tests on the blood and urine, blood cholesterol determinations, and basal metabolic tests when the cooperation of the patient permits. Medication should be started with small doses and gradual increases instituted until the maintenance dosage is reached. Two case reports are included.

MARSHALL, San Francisco.

STUDIES OF THE NATURE OF ANTIGONADOTROPIC SUBSTANCES. G. H. TWOMBLY, Endocrinology **20**:311 (May) 1936.

The fact that long-continued injection of certain hormonal preparations results in loss of reactivity in the experimental animal and in the formation, in the serum of the animal, of substances capable of neutralizing the effects of the hormones has been demonstrated by Collip and his co-workers.

Twombly reports that he was successful in producing a similar substance opposed to both the gonadotropic hormone found in the urine of patients suffering from teratoma testis and the gonadotropic hormone in the urine of pregnant women, so that the serums of animals given injections of it protected infantile mice against the luteinizing action of this hormone, even though five times the minimal luteinizing dose was administered.

The purpose of the experiments described was to determine whether these substances are truly antihormonal, having an effect opposite to that of the hormones injected, or whether they are simply protein antibodies which unite with protein antigens intimately connected with the hormones, precipitate these and thereby carry the hormones out of solution.

The conclusions were as follows: It seems probable that these substances are protein antibodies formed by injection of foreign proteins, since precipitins for the hormones as antigens can be demonstrated in the immune serums and seem to

parallel the protective properties of the serums; since hormones partially inactivated by heat or completely so by aging seem to be about as efficient in bringing about the formation of these protective substances as active preparations of the hormones; since no antihormone has been found in the blood of three patients given injections of large quantities of the hormone for two weeks, six weeks and over a year, and finally since long-continued injection of large doses of a nonprotein hormone, the estrogenic hormone, into rabbits failed to result in the formation of any such protective substances.

JACOBSEN, Buffalo.

THE BIOLOGIC EFFECTS OF THYMECTOMY: ACCRUING RETARDATION IN GROWTH IN SUCCEEDING GENERATIONS. N. H. EINHORN and L. G. ROWNTREE, Endocrinology **20**:342 (May) 1936.

Accruing acceleration in the rate of growth and development occurs in young rats when successive generations of parents are given daily intraperitoneal injections of 1 cc. of a potent extract of thymus. In this paper the effect of removal of the gland in successive generations is described.

Thymectomy performed on young rats exercised no recognizable influence on their further growth and development but resulted in definite retardation in the rate of growth in over 300 albino rats of the second and third generations. The average retardation in growth at its maximum was 36.9 per cent at thirty days after birth, slightly greater in the third generation than in the second. After seventy days the curves of growth conformed to normal.

When thymectomized rats were given daily injections of 1 cc. of thymus extract the growth curves of the young coincided closely with those of normal control animals.

JACOBSEN, Buffalo.

THE BIOLOGICAL EFFECTS OF PINEAL EXTRACT (HANSON): ACCRUING RETARDATION IN GROWTH AND ACCRUING ACCELERATION IN DEVELOPMENT IN SUCCESSIVE GENERATIONS OF RATS UNDER CONTINUOUS TREATMENT WITH PINEAL EXTRACT. L. G. ROWNTREE, J. H. CLARK, A. STEINBERG and A. M. HANSON, Endocrinology **20**:348 (May) 1936.

The success attending the authors' studies with the continuous administration of an extract of thymus to successive generations of parent rats, resulting in remarkable precocity in the offspring of the third and succeeding generations, led them to carry out the same procedure with an extract of the pineal gland.

Administration of pineal extract, 1 cc. intraperitoneally daily, tends to increase the frequency of breeding, to decrease the weight at birth and the rate of growth and to accelerate the rate of differentiation and development. The effect on the young becomes more marked in succeeding generations. In the fifth generation the average young rat was less than 50 per cent of the normal weight, was sexually mature in less than half the normal time and evidenced marked precocity from the standpoint of the development of fur, eruption of teeth, opening of eyes, etc.

JACOBSEN, Buffalo.

THE PRESENCE OF AN EXCESS OF 'MALE' (COMB-GROWTH AND PROSTATE-STIMULATING) HORMONE IN VIRILISM AND PSEUDO-HERMAPHRODITISM. S. LEVY-SIMPSON, P. DE FREMERY and A. MACBETH, Endocrinology **20**:363 (May) 1936.

It has been found that there is present in the urine of normal women a substance capable of stimulating comb-growth in capons, this substance being very similar to or identical with testicular hormone. The present investigation was undertaken to ascertain whether the development of male secondary sex characters (virilism) in the female is associated with secretion of an excess of androgenic hormone.

Tests were made with the urine of fourteen patients to determine the amount of this hormone present as measured by comb growth in capons and prostate growth in castrated rats.

An excess of androgenic hormone was found in four of seven women with an adrenogenital syndrome and in three women with Cushing's syndrome. No excess was found in women over 50 years of age with Achard-Thiers syndrome or in three of the seven women with the adrenogenital syndrome.

The chief interest to pediatricians lies in the report on three pseudohermaphrodites aged 10, 16, and 4 years, respectively, in two of whom an excess of androgenic hormone was found.

The authors leave open the question as to whether excess of this hormone causes virilism or is only one of its manifestations. JACOBSEN, Buffalo.

CHILDHOOD MYXEDEMA: OBSERVATIONS THROUGH INFANCY, CHILDHOOD AND EARLY ADULT LIFE. C. G. KERLEY, Endocrinology **20**:611 (Sept.) 1936.

Eight cases of congenital hypothyroidism are reported, all followed from early childhood for periods of from ten to thirty-five years. Photographs demonstrate the improvement brought about by the administration of thyroid. The importance of varying the dose according to the clinical response is emphasized, one patient requiring 1 or 2 grains (0.065 or 0.13 Gm.) daily in infancy, from 12 to 15 grains (0.776 to 1 Gm.) during adolescence and but 2 grains at the age of 35 years.

Apathy, indolence, increase in weight and dryness of the skin are the call for more thyroid; sleeplessness, irritability, perspiration, tachycardia and loss in weight indicate the necessity for reduction. Early recognition and continuous supervision are required for the best results. JACOBSEN, Buffalo.

CREATINE STUDIES IN THYROID DISORDERS. G. W. THORN, Endocrinology **20**:628 (Sept.) 1936.

The creatine tolerance test was employed in a study of twelve patients with thyrotoxicosis and seven with myxedema.

Impairment in the retention of creatine was noted in all the patients with thyrotoxicosis; iodine reduced creatinuria and improved retention, but proof of a primary effect of iodine on the metabolism of creatine is lacking.

In myxedema administration of thyroid decreased the retention of creatine, creatinuria often preceding the metabolic rise.

The degree of creatinuria is useful in determining the physiologic dosage of thyroid for patients with spontaneous myxedema and for totally thyroidectomized patients with cardiac disease.

Attempts to reduce the creatinuria in thyrotoxic patients by administering adrenal cortical hormone were unsuccessful. JACOBSEN, Buffalo.

FUNDAMENTAL FACTORS IN THE INTERPRETATION OF STIMULI INFLUENCING ENDOCRINE GLANDS. H. SELYE and J. B. COLLIP, Endocrinology **20**:667 (Sept.) 1936.

Large doses of an estrogenic substance (theelin) caused hypertrophy of the adrenal cortex of the corpus luteum and of the mammary gland in normal but not in hypophysectomized animals. Even when these glands were prevented from atrophying following hypophysectomy by injections of anterior pituitary extracts, subsequent injections of the estrogenic substance were without effect on the adrenal cortex or the mammary gland. But definite enlargement of the ovaries was produced. The conclusion is that the substance in question, besides its stimulating action on the pituitary, has a direct effect on the ovary, while it has no direct effect on the adrenal or on the mammary gland.

Similarly formaldehyde was found to affect the adrenal cortex only in the presence of the pituitary gland.

Further experiments indicated that both the ovary and the pituitary gland remain fully responsive to gonadotropic stimuli in animals malnourished because of deficient diets. JACOBSEN, Buffalo.

Relation Between the Occurrence of Endemic Goiter and the Presence of Traces of Silver and Barium in Drinking Water. C. H. Boissevain and W. F. Drea, Endocrinology **20**:686 (Sept.) 1936.

While it is generally admitted that deficiency of iodine is the primary cause of endemic goiter, any factor that interferes with the utilization of the iodine present may constitute a secondary cause. The finding by spectroscopic examination of strong traces of silver in water from goitrous regions in America and large amounts of barium in water from the Swiss region of goiter suggested feeding experiments to determine the effect of these metals on animals.

Such experiments on twenty rats failed to reveal any influence of either silver or barium on the development of goiter. Jacobsen, Buffalo.

Adrenal Virilism. W. Saphir and M. L. Parker, J. A. M. A. **107**:1286 (Oct. 17) 1936.

A girl of 15 years presented sudden amenorrhea, rapid gain in weight, hirsutism and deepening of the voice. At operation the kidneys and adrenal glands were found to be normal. The right ovary, which was somewhat enlarged and showed three cysts, was removed. Histologic examination revealed aberrant adrenal cortex in the ovary. Embryologically, adrenal cortex, ovaries and testes have a common origin, so that aberrant rests of adrenal cortex may be found in the gonads. Therefore, the presence of normal adrenal glands does not rule out adrenal virilism, and removal of the normal-sized adrenal gland would be not only futile but dangerous. After operation the patient resumed her normal menstrual cycle in five days, and the increased estrogenic excretion present before operation disappeared. Bonar, Salt Lake City.

Parathyroid Hormone in the Blood of Pregnant Women. Bengt Hamilton, Laura Dasef, Walter J. Highman Jr. and Charles Schwartz, J. Clin. Investigation **15**:323 (May) 1936.

The report summarizes the results from determinations of the parathyroid hormone in the blood of thirty normal, seventy-four pregnant and eleven lactating women. The hormone was frequently found to be higher than normal from the fifteenth to the thirty-fifth week of pregnancy. The method of the test used in this study has been described by Hamilton and Highman (*J. Clin. Investigation* **15**:99, 1936). Guest.

Certain Relations Between the Parathyroids, the Hypophysis and the Pancreas. Bernard A. Houssay, New England J. Med. **214**:1128 (June 4) 1936.

This paper covers a study of the microscopic aspect of the parathyroids and also of the blood calcium of (*a*) hypophysectomized, (*b*) pancreatectomized and (*c*) hypophysectomized-pancreatectomized dogs.

In the presence of pituitary insufficiency in the dog there is cellular atrophy in the parathyroids, with foci or zones of accumulated nuclei, which simulate cords and occasionally acellular basophilic areas. These changes may be the result of general nutritive alterations or of the lack of parathyrotropic hormone.

The blood calcium is not altered, probably because the parathyroid lesion is partial or incomplete.

Anterior pituitary extract increases the size of the parathyroids and their content of clear cells. It also raises the level of the blood calcium; but this rise does not occur when the parathyroids have been removed. Pituitary extracts do not prevent or cure the hypocalcemia and tetany due to parathyroidectomy, and the results following thyroparathyroidectomy are similar in hypophysectomized and in normal dogs. In pancreatic insufficiency in the dog there are vacuolation, liquefaction and later protoplasmic disintegration of the cells of the parathyroids. The

nuclei remain isolated, forming tubes, rows or islets. In from three to seven days the blood calcium is lowered to levels between 7 and 9 mg. per hundred cubic centimeters of plasma, and the blood phosphorus increases. Insulin prevents the decrease of the blood calcium, but in experiments late treatment with insulin, after the fall in calcium had occurred, was not completely effective in raising the level of calcium to normal, nor was the normal histologic appearance of the glands restored.

GENGENBACH, Denver.

THE HYPOPHYSIS AND RESISTANCE TO INTOXICATIONS, INFECTIONS AND TUMORS. BERNARD A. HOUSSAY, New England J. Med. **214**:1137 (June 4) 1936.

Those particularly interested in this subject should read the original article with its remarkable bibliography containing nearly 300 references, as it does not lend itself well to being abstracted.

The existence of a direct antitoxic or anti-infectious action of the pituitary gland or of its secretions has not been proved, but the gland can modify the resistance of the animal by its metabolic action, by its regulating action on the thyroid or on the adrenal gland and by its action on the vascular and nervous systems.

The gland can show certain histologic changes during infections or intoxications, but the functional significance of the changes is not understood. Anesthetics and hypnotics are not tolerated well by hypophysectomized animals, and after hypophysectomy some species are more susceptible to infections. This operation through producing hypothyroidism, provokes a decrease in phagocytosis and accelerated formation of antitoxin (in dogs), the production of agglutinins not being changed. The thyrotropic hormone of the anterior lobe of the pituitary gland, by stimulating activity of the thyroid gland, causes hypersensitiveness to anoxemia in rodents. In the mouse an increase in resistance to acetonitrile, and in the dog a slight increase in resistance to chloralose (a dextrose derivative of chloral) occurs.

The pituitary gland can be the site of a benign or a malignant new growth, also of a metastasis. Hypophysectomy retards but does not prevent the growth of tumors and diminishes the number of implantations which take; probably this is due to a metabolic action, which should be studied.

GENGENBACH, Denver.

MYXEDEMA FOLLOWING THE REMOVAL OF AN ABERRANT THYROID TUMOR. J. G. PROBSTEIN and HARRY AGRESS, New England J. Med. **214**:1191 (June 11) 1936.

Profound disturbances in thyroid metabolism, such as myxedema, are frequently attendant on removal of median aberrant thyroid tissue. This phenomenon is strikingly in contrast with what follows extirpation of lateral aberrant thyroid tissue. The discrepancy is best explained by differences in embryonic development. The authors report a case in which a 17 year old white girl complained of a swelling which had been present for two weeks just to the right of the midline in the sublingual region. Her past history was interesting in that it was one of retarded development in infancy and early childhood. Her first teeth appeared at the age of 2 years, and she did not start to walk or talk until the age of 4. She was always somewhat retarded mentally as compared with other children in the family. Her menses started at the age of 17 years and were irregular, scanty and painful.

Exploratory operation was advised on the basis of the following clinical diagnoses: (*a*) submental lymph gland, (*b*) suspected obstruction of the sublingual ducts, (*c*) hygroma and (*d*) thyroglossal duct cyst. Operation was performed under

gas-ether anesthesia. A spherical soft tumor, approximately 3 cm. in diameter, was found superior and superficial to the right wing of the hyoid bone. The mass was completely excised, and the incision was closed by routine methods. Exploration for normal thyroid tissue was not carried out.

*Pathologic Report.*—The diagnosis was aberrant thyroid papillary cyst adenoma. Four months later the patient presented the classic picture of myxedema and complained of ready fatigability, dulness, chilliness and costiveness. She had been amenorrheic for three months. Her pallor was marked, and the skin, which was dry, cracked and scaly, had a yellowish tinge. The basal metabolic rate was minus 32 per cent.

She was given 1 grain (0.064 Gm.) of thyroid extract twice daily, with rapid and persistent improvement as long as she adhered to the replacement therapy.

GENGENBACH, Denver.

MAINTENANCE OF CARBOHYDRATE LEVELS IN FASTED HYPOPHYSECTOMIZED RATS TREATED WITH ANTERIOR PITUITARY EXTRACTS. JANE A. RUSSELL and L. L. BENNETT, Proc. Soc. Exper. Biol. & Med. **34**:406 (May) 1936.

Hypophysectomized rats previously were found to have an abnormal decrease of glycogen in the blood, liver and muscle when starved. The administration of an extract of anterior pituitary prevented the drop in carbohydrate to these low levels in these tissues during the intervals of starvation. This action of the "glycostatic" factor in anterior pituitary was not affected by previous removal of the adrenal glands.

HANSEN, Minneapolis.

THYROID DISEASE AND BLOOD LIPIDS. E. M. BOYD and W. F. CONNELL, Quart. J. Med. **5**:455 (Oct.) 1936.

Boyd and Connell studied the blood lipids in nine cases of hyperthyroidism and in five cases of hypothyroidism observed at the Kingston General Hospital, Kingston, Ontario, Canada. A modification of the Bloor oxidative microtechnic was used.

In hyperthyroidism plasma lipids were found decreased in value by approximately a third on the average, but no consistent increase was found in hypothyroidism.

As thyroid function increased, plasma lipids decreased in the following relative order: neutral fat > cholesterol esters > free cholesterol > phospholipid. The lipid composition of the red cells in patients with thyroid disease was within the normal range. The authors suggest that the variations in the plasma lipids in thyroid disease are due to the effect of the thyroid hormones themselves and not indirectly to the change these produce in the basal metabolic rate.

BRADFORD, Rochester, N. Y.

DIABETES MELLITUS IN INFANCY. C. L. HOLLAND and E. A. HOLLAND, West Virginia M. J. **32**:407 (Sept.) 1936.

After a brief review of the literature on the subject, the Hollands report a case of diabetes mellitus in a prematurely born infant 13 months old, who had been under their care since the discovery of the condition—a period of five months. At the time of the report the baby, a girl, weighed 14¼ pounds (6,350 Gm.), and presented the appearance of normal health. She was on a controlled diet and was receiving 3 units of insulin three times daily. The urine was sugar-free.

SHAWKEY, Charleston, W. Va.

PRESENT POSITION OF ENDOCRINOLOGY. W. L. BROWN, Brit. M. J. **2**:772 (Oct. 17) 1936.

This is a general discussion of the subject of endocrinology with special reference to "we know" and "we don't know." It contains a caution as to indiscriminate use of hormonal therapy without more accurate knowledge than is possessed at present.

ROYSTER, University, Va.

STUDIES ON ENDEMIC AND EXPERIMENTAL GOITRE. C. E. HERCUS and H. D. PURVES, J. Hyg. **36**:182 (June) 1936.

Since Prevost in 1830 formulated the theory that goiter is due to lack of iodine there has been a dispute about the exact rôle of the deficiency, but in general "a low intake of iodine is a prerequisite for high goiter incidence." While there are other factors, such as infections, deficiencies of the vitamins and dietetic influences, a lack of iodine is the important factor.

Lunde found that the highest daily urinary excretion of iodine in a region of goiter is 87 micrograms. The lowest excretion for any area described by the authors as nongoitrous (Switzerland, Norway, Holland or New Zealand, for instance) is 112 micrograms per day. It is assumed that the urinary excretion is about 70 per cent of the intake. Hence, theoretically, the necessary intake is computable and given as between 120 and 160 micrograms per day. Computations made on the urinary excretion of iodine for the various regions show that the incidence of goiter is parallel to the deficiency in iodine. Authors who have reported unsatisfactory results from the use of iodine have had such results because the amount of iodine given has been insufficient.

In New Zealand, especially, the studies showed that since 1923, when the recommendation of iodized salt was first made, its employment has been slow, the amount used constituting only 30 per cent of the amount of domestic salt used. Also the iodine content of 2 parts of potassium iodide to 250,000 parts of salt is too small. The authors recommend that the ordinary domestic salt be iodized with from 5 to 6 parts of potassium iodide to 250,000 parts of salt, and that noniodized salt be so labeled, with the addition, "The use of this salt exposes the user to the risk of developing goiter."

Their experimentation on animals showed that among goitrogenic foods (cabbage, turnips, etc.) rape seed is quite active, and that such activity is destroyed by steaming. They believe that such goitrogenic activity is caused by glucosides.

JANNEY, Wauwatosa, Wis.

IMPAIRMENT OF ANTERIOR PITUITARY FUNCTIONS BY FOLLICULAR HORMONE. B. ZONDEK, Lancet **2**:842 (Oct. 10) 1936.

Prolonged administration of follicular hormone was found to interfere with the functions of the anterior lobe of the pituitary gland. Rats and chickens were used in these experiments. Not all the functions of the anterior lobe are affected equally. The gonadotropic function is the most sensitive. Failure of the growth hormone follows failing of the gonadotropic hormone.

LANGMANN, New York.

OBSERVATIONS UPON THE METABOLISM OF CALCIUM AND PHOSPHORUS IN THREE CASES OF ACROMEGALY, ONE SHOWING OSTEOPOROSIS. L. B. COX and I. M. MCPHEE, M. J. Australia **2**:390 (Sept. 19) 1936.

The metabolism of calcium and phosphorus in three acromegalic persons was investigated, and no abnormality was detected. In one of these patients considerable rarefaction of bone was present.

GONCE, Madison, Wis.

THE RELATIONSHIP OF THE IODINE CONTENTS OF WATER, MILK AND PASTURE TO THE OCCURRENCE OF ENDEMIC GOITER IN TWO DISTRICTS OF ENGLAND. M. G. CRABTREE and E. M. MASON, Medical Research Council, Special Report Series, no. 217, London, His Majesty's Stationery Office, 1936.

The authors conducted a survey of school girls between the ages of 6 and 14 years for thyroid enlargement, in two English counties. The county that had the greatest incidence of goiter had the greatest deficiency of iodine in the water. This deficiency is not believed to be the whole cause. The availability of iodine in the soil to herbage and hence to animal population may be a complicating factor.

SANFORD, Chicago.

INFANTILE MYXOEDEMA. K. H. TALLERMAN, Proc. Roy. Soc. Med. **29**: 1436 (Sept.) 1936.

A case of myxedema in a child aged 5 years is reported. The report is accompanied by a picture of the patient.

WILLIAMSON, New Orleans.

EXTRACT OF THE HYPOPHYSIS IN THE TREATMENT OF DIABETES INSIPIDUS. P. LEREBOULLET and J. BERNARD, Arch. de méd. d. enf. **39**:421 (July) 1936.

Exhaustive clinical reports of three cases of diabetes insipidus, two in boys of 6 and 4 years and the other in a girl of 12 years, are reviewed and the observations summarized. These patients were followed for years, and an extract of the posterior lobe of the hypophysis given subcutaneously daily in doses of 1 cc. proved most efficacious in controlling the diuresis; the diminution of the polyuria always preceded the decrease in the polydipsia. Lereboullet and Bernard stress the vital importance of differentiating the pure symptomatic type of this disease from the diabetes associated with gross pathologic changes in the hypophysotuberian region.

AMESSE, Denver.

TUMOR OF THE HYPOPHYSIS. J. ROUDINESCO, Arch. de méd. d. enf. **39**:450 (July) 1936.

The clinical aspects of tumor of the hypophysis are of such extreme diversity that one finds neoplasms of this structure represented by such unlike syndromes as those exhibited in acromegaly, dystrophia adiposogenitalis and Cushing's disease.

This clinical polymorphism is further associated with disturbances of varying degree due to pressure on neighboring tissues, such as the optic tracts, the infundibulo-tuberian centers and the structures composing the third ventricle. Tumors are likewise responsible for general intracranial pressure and for functional glandular derangement.

An exhaustive treatise on this complex subject is presented, in which Roudinesco discusses the history, etiology, occurrence, pathologic anatomy, clinical course and diagnosis of tumor of the pituitary body.

AMESSE, Denver.

MYXEDEMA WITH HYPOCHROMIC ANEMIA AND HYPERCHOLESTEREMIA IN A CHILD. S. B. BRISKAS, Arch. de méd. d. enf. **39**:591 (Sept.) 1936.

A case representing this syndrome together with statural hypotrophy and mental deficiency is presented by a member of the Faculty of Medicine of Paris. The patient was a girl 4 years old. At the age of 2½ years she showed a sudden arrest of growth; she was treated for rickets and sent to a health resort. Two years later, retardation, physical and psychic, was manifest; thyroid insufficiency was diagnosed, and specific treatment with a powdered extract, given orally, was instituted. In a few months the patient was literally transformed.

The literature on myxedematous anemia is carefully reviewed.

AMESSE, Denver.

A Case of Pharyngeal Asphyxia in a Girl Four Years Old with Exophthalmic Goiter. Louis Leroux and E. Welti, Bull. Soc. pédiat. de Paris **33**:515 (June) 1935.

A girl 4 years old, who had exophthalmic goiter, acquired acute asphyxia. When a laryngoscope was passed, no abnormality was found beyond the pharynx, but the difficulty in breathing subsided. It became evident that the obstruction to respiration was due to huge, inflamed tonsils and falling back of the base of the tongue. The child required the introduction of a Mayo tube into the throat every night for three nights, although she was better during the day. As the tonsillitis subsided, she recovered. The goiter was not large enough to cause obstruction.

Benjamin, Montreal, Canada.

The Metabolism and Importance of Iodine in the Young Organism. IV. Relation Between the Iodine of the Blood and the Glands of Internal Secretion—Thyroid, Parathyroid, Thymus, Adrenal. E. Piras, Riv. di clin. pediat. **34**:908 (Oct.) 1936.

Piras' observations were on dogs. Following thyroidectomy there was lowering of the iodine level of the blood, with disappearance of the usual individual variations. Similar diminution in the iodine was found following parathyroidectomy. Thymectomy, on the contrary, led to increase, noticed after twenty-four hours and persisting for at least seven days. The giving of epinephrine hypodermically caused an increase lasting from three to twenty-four hours and varying according to the dose given.

Higgins, Boston.

The Thymus Gland and Bone Regeneration. A. Haas and H. Hanke, Deutsche Ztschr. f. Chir. **247**:724 (Oct. 23) 1936.

The literature on this subject is reviewed briefly, and the uncertainty of a relationship of the thymus gland to bone regeneration is pointed out. This uncertainty is due to the absence of a demonstrable hormone and to experimental errors resulting from unsatisfactory technic. The authors' method is to drill holes in the radial bones of rabbits of the same litter between the ages of 8 and 16 weeks. Regeneration is compared in different rabbits and in the same rabbit before and after thymectomy. Complete removal of the thymus gland of the rabbit is not difficult. The authors were unable to demonstrate any relationship between the presence or absence of the thymus gland and bone regeneration. Administration of an extract of the thymus gland (the thymocresein of Asher, made by Ciba) had no demonstrable effect.

Glaser, Rochester, N. Y.

Roentgenographic Support of the Clinical Diagnosis of Sporadic Cretinism. R. W. Müller, Fortschr. a. d. Geb. d. Röntgenstrahlen **53**:877 (June) 1936.

The roentgenographic features of the skeleton of the cretin are described briefly. Two cases of juvenile hypothyroidism are reported, with well reproduced illustrations. The roentgenograms of the second patient suggest achondroplasia more strongly than cretinism.

McCune, New York.

Thyroid and Rickets. F. Thoenes, Jahrb. f. Kinderh. **145**:177 (Oct.) 1935.

Thoenes found that thyroid substance had no beneficial healing effect on infantile rickets. The same results were found experimentally, rats being the animals used. He was unsuccessful in producing rickets by operative removal of the thyroid glands of 3 week old rabbits.

Landau, Hannibal, Mo.

ADDISON'S DISEASE IN A CHILD. GEORG OSKAR HARNAPP, Monatschr. f. Kinderh. **66**:213 (July) 1936.

Harnapp reports the case of a 12 year old boy, in whose family there seemed to be some abnormality of the adrenal system. He was treated with adrenal cortical substance, sodium chloride and cevitamic acid. Vitamin C exerted the most beneficial effect on the pigmentation. The influence of the salt was inconclusive. The treatment with adrenal cortex hormone seemed more successful when the preparation was given by mouth than when it was given subcutaneously.

GERSTLEY, Chicago.

SUGAR TOLERANCE CURVES IN THE FAMILIES OF DIABETIC CHILDREN. GERTRUD PHILIPP-LUNSMANN, Monatschr. f. Kinderh. **67**:20 (Sept.) 1936.

In an attempt to determine whether there was a familial tendency toward diabetes, Philipp-Lunsmann determined the sugar tolerance of the immediate families of her diabetic patients. In some cases she doubled the load of sugar. Unquestionably, the relatives of the diabetic patients, even on the simple test, showed delayed return of the curve to normal. Of those receiving a double load, many showed a second increase in the curve to a height greater than that of the first rise. These deviations from normal were found only in the female relatives. In eight of eleven families studied, these changes were found in the relatives of the parents' generation.

GERSTLEY, Chicago.

THE SYNDROME OF THE PRECOCIOUS GENITAL DEVELOPMENT OF POSTENCEPHALITIC ORIGIN. A. RADOVICI, Bull. Acad. de méd. de Roumanie **1**:194, 1936.

Radovici discusses the evidence supporting the concept of a regulation of growth and sexual development by the pineal gland. Literature is cited which suggests that neoplastic or inflammatory processes may disturb pineal function. The case reported is that of a 15 year old girl who had had an illness diagnosed as meningitis when she was 1½ years of age. Early in childhood she began to show abnormal sexual development, disproportionate growth between the trunk and the extremities, and mental retardation. At 14 years she began to have severe convulsive seizures. No attempt was made to explain the hypertension which the child showed, and inasmuch as roentgenograms of the skull were the only x-ray pictures reported and the spinal fluid pressure was not recorded, the reviewer feels that neither an adrenal nor an intracranial tumor was ruled out.

DIETRICH, Los Angeles.

ADRENAL CORTICAL SYNDROME IN A PATIENT WITH TUMOR OF AN ACCESSORY ADRENAL GLAND. B. JOSEPHSON, Acta med. Scandinav. **90**:385, 1936.

A 17 year old boy showed nearly all the symptoms characteristic of basophilic adenoma of the pituitary gland or of tumor of the cortex of the adrenal gland except hyperglycemia. X-ray pictures showed that the sella turcica was normal but that there was a calcifying tumor at the upper pole of the left kidney. After removal of the tumor, which was the size of a hen's egg and made up of adrenal cortex, the blood pressure dropped from 180 to 70 mm. Despite administration of cortical hormone, intravenous injection of saline solution and transfusion of blood, the patient died nineteen hours later. Postmortem examination showed both adrenal glands in the normal sites and atrophic, the cortex without lipids and the hypophysis normal.

KAJDI, Baltimore.

THE HEPATIC GLYCOGEN AFTER ADRENALECTOMY IN RATS. G. WIDSTROEM, Acta med. Scandinav. **90**:397, 1936.

In adrenalectomized rats three or four days after operation the glycogen in the liver is only a tenth to a half of that observed in control animals; administration of cortical hormone or high intake of salt prevents this drop in glycogen.

Adrenalectomized rats suffer a drop of from 8 to 10 C. in body temperature when exposed to low temperatures (3 to 17 C.) for several hours; administration of salt prevents this drop.

KAJDI, Baltimore.

ELEVEN CASES OF CONGENITAL STRUMA. C. E. RÄIHÄ, Acta pædiat. **19**:50, 1936.

In the course of a single year (1935) eleven patients with congenital struma were encountered in the University Pediatric Clinic, Helsingfors, Finland; all of these patients came from a vicinity where goiter is peculiarly common. The struma was usually diffuse; however, in two instances a relatively large adenoma was felt. In all cases the history was elicited that struma had developed in the mother during the pregnancy at the end of which the infant was born. A history of goiter in other members of the family was obtained more frequently among these eleven infants than among infants who did not have enlargement of the thyroid gland at birth. In eight of the patients the enlarged thyroid gland caused moderate dyspnea, which was easily controlled by extension of the head and by use of sedatives. The gland remained enlarged for only a few weeks; respiratory symptoms diminished before the struma had disappeared. Large doses of iodine did not appear to accelerate the return to normal. Those patients who were simply kept in the hospital without formal medicinal treatment improved as rapidly as those who received iodine. A conjectural explanation of this phenomenon is the fact that the infants were freely exposed to the vapors emanating from flasks of tincture of iodine which are kept in each ward of the hospital not far from the patients. Räihä concedes the importance of environmental circumstances in the pathogenesis of congenital struma but emphasizes his conviction that hereditary and familial factors must also be taken into account.

MCCUNE, New York.

INFLUENCE OF ZINC ACETATE ON THE EFFECT OF INSULIN IN DIABETES. U. CARLBORG, Svenska läk.-sällsk. handl., 1936, no. 8, p. 220.

Zinc acetate added in the proportion of 0.1 per cent to ordinary insulin retards the resorption of the insulin and thus prolongs its effect. The injection of this compound causes no local inconvenience and no untoward symptoms. The lowering effect on the blood sugar lasts several hours longer than that of ordinary insulin, and the initial drop in the blood sugar level is smaller. A comparison of the effect of zinc-insulin with that of insulin protaminate showed that these compounds are of about the same value in the treatment of diabetes.

WALLGREN, Göteborg, Sweden.

HYPERINSULINISM OF THE NEW-BORN IN A CASE OF DIABETES MELLITUS. J. A. M. J. ENNEKING, Nederl. tijdschr. v. geneesk. **80**:3351 (July 18) 1936.

Enneking reports a case of severe diabetes in a woman, two of whose children died soon after birth, probably from hypoglycemia caused by hyperinsulinism. A third child was given prophylactic doses of dextrose orally and subsequently developed regularly.

VAN CREVELD, Amsterdam, Netherlands.

## Diseases of the Muscles, Bones, Joints and Lymph Glands

PHYSIOLOGIC EFFECTS OF THE CORRECTION OF FAULTY POSTURE. L. B. LAPLACE and J. T. NICHOLSON, Am. J. M. Sc. **192**:345 (Sept.) 1936.

Eighteen healthy subjects with postural defects of the kypholordotic type were studied with respect to the immediate physiologic changes produced by correction of posture. Correction of posture did not always produce an elevation of the diaphragm with respect to the top of the chest nor did the heart always become more transversely placed. The cause and significance of these facts are discussed.

The vital capacity was increased by assuming a correct posture. The respirations in the corrected posture became slower and deeper, and the respiratory minute volume was increased. The consumption of oxygen was not altered in a consistent manner, but there was suggestive evidence that under normal conditions it is lower in the corrected than in the faulty posture. Changes in the blood pressure and pulse rate on standing indicated in the majority of subjects a better degree of circulatory efficiency in the corrected posture.

It was concluded that the correction of postural defects has a significantly beneficial effect on circulatory and respiratory function in the majority of subjects. For each patient there is an optimal posture, the attainment of which produces the maximum therapeutic benefit.

HENSKE, Omaha.

XANTHOMATOSIS (SCHÜLLER-CHRISTIAN DISEASE). R. A. STRONG, J. A. M. A. **107**:422 (Aug. 8) 1936.

The terms "xanthomatosis" and "Schüller-Christian disease" are usually used to describe a syndrome consisting chiefly of three clinical features. These are defects of the skull, diabetes insipidus and exophthalmos. The less frequent symptoms are gingivitis, dwarfism, defects of the skeleton and occasional adiposogenital dystrophy. While the absence of one or more of these symptoms does not rule out the condition, defects of the skull must be present to make a diagnosis. Rowland's explanation seems to be the most plausible: a disturbance of the lipoid metabolism with an occasional but inconstant increase in blood cholesterol and later a deposition of lipoids chiefly in the form of cholesterol or its esters in the various organs and tissues of the body as well as in the reticulo-endothelial system. Management of the diet and roentgen treatment of the areas of lipoid deposit offer the most hope of improvement. The defects in the skull and skeleton are benefited by this treatment, but the exophthalmos is not.

BONAR, Salt Lake City.

BRODIE'S ABSCESS OF RADIUS, DUE TO TYPHOID. W. B. MARBURY and H. L. PECKHAM, J. A. M. A. **107**:1284 (Oct. 17) 1936.

Typhoid of the bones is an unusual type of bone disease. Marbury and Peckham report the case of a girl of 15 years who developed Brodie's abscess in the lower radius, from the pus of which Bacillus typhosus was cultured. The patient gave a history of having had typhoid fever ten years before. Incision and drainage produced a cure.

BONAR, Salt Lake City.

ACUTE OSTEOMYELITIS IN CHILDREN. R. T. FINDLAY, New York State J. Med. **36**:1231 (Sept. 1) 1936.

Findlay reports on 105 children with osteomyelitis. Of these, 55 had chronic and 50 acute lesions. The etiology, pathology, diagnosis, complications and treatment are discussed. The mortality was 24 per cent. Findlay is of the opinion that "simple incision through the periosteum is probably the operation of choice in a large majority of cases."

AIKMAN, Rochester, N. Y.

THE OSSIFICATION OF THE CARPUS IN RICKETS, CONGENITAL SYPHILIS AND CRETINISM. P. MACARTHUR, Arch. Dis. Childhood **11**:243 (Oct.) 1936.

The reports and x-ray plates in 211 cases of active rickets in children under 5 years of age, 14 cases of congenital syphilis and 20 cases of cretinism were examined to determine whether ossification in the three diseases is normal or delayed.

These records indicate that ossification is almost invariably delayed in cretinism, frequently advanced and seldom delayed in congenital syphilis, and delayed in rickets in about 25 per cent of the cases. In view of the delay in the appearance

of the carpal centers of ossification in some cases of rickets without any signs of hypothyroidism, it does not seem justifiable to claim that this is in itself diagnostic of congenital thyroid deficiency. KELLY, Milwaukee.

AMYOPLASIA CONGENITA ASSOCIATED WITH MONGOLISM. L. C. COOK, Arch. Dis. Childhood **11**:261 (Oct.) 1936.

A child of 7½ years with many of the features of amyoplasia congenita is described in detail. The main features of amyoplasia congenita are:

1. Congenital rigidity of joints of varying degrees, usually symmetrical and always without inflammatory change.

2. Hypoplasia or degeneration of those muscles which normally produce the movements which the child is unable to perform.

3. Absence of any hypertonia or hypertrophy of antagonistic muscles, showing that the immobility is not attributable to muscular overaction.

4. Sudden checking of movement at the affected joints so that no application of force can increase movement, which points to bony or fibrous changes in the structures of the joint. The fact that mobility is not increased under general anesthesia corroborates the last two points.

5. Weakness or absence of faradic responses in affected muscles, but no reaction of degeneration.

6. Absence of sensory or trophic changes.

7. Normal intelligence.

8. Extensive fibrous-fatty changes in the affected muscles.

KELLY, Milwaukee.

MYOPATHY. J. V. BRAITHWAITE, Proc. Roy. Soc. Med. **29**:1439 (Sept.) 1936.

A case in a child of 5 years is reported. There was no family history of myopathy or paralysis. WILLIAMSON, New Orleans.

OSTEOCHONDRITIS OF THE CAPITELLUM. L. J. RAE, Proc. Roy. Soc. Med. **29**:1660 (Oct.) 1936.

A case is reported in a child of 8 years. WILLIAMSON, New Orleans.

OSTEOCHONDRITIS OF THE LOWER END OF THE LEFT FEMUR IN A CHILD AGED FIVE YEARS. E. L. EVANS, Proc. Roy. Soc. Med. **29**:1665 (Oct.) 1936.

A case is reported in a girl of 5 years. Pain and swelling commenced in the left knee about two months after a wrenching of the left leg. This pain continued until the child was brought to the hospital about four months later. The knee at this time showed free fluid in the joint, with a floating patella. The Wassermann and Mantoux reactions were negative. Three months later in spite of open-air treatment and fixation on a plastic splint, some fluid remained in the joint, with tenderness. Six months later there was no swelling, pain or tenderness. A series of roentgenograms was taken, and reproductions of these accompany the report. WILLIAMSON, New Orleans.

CHONDRODYSTROPHIES. A. RICHARD, P. V. DUPUIS, C. ROEDERER and R. FROYEZ, Rev. d'orthop. **23**:490 (Sept.) 1936.

Multiple exostosis, chondromatosis and Ollier's dyschondroplasia constitute three types of dystrophy of bone characterized by abnormal deposits of cartilage at the metaphysial lines of the long bones and in the small bones of the extremi-

ties, which deposits show slow ossification. All three types should be classified under one term, "Chondrodystrophy." The authors append the following table:

| | Dyschondroplasia | Multiple Exostosis | Chondromatosis |
|---|---|---|---|
| Date of appearance | Early infancy | Later infancy | Early infancy |
| Sex involved | Female | Male | Male chiefly |
| Heredity | Not inherited | Very frequently inherited | Frequently inherited |
| Hands | Least involved | Involvement discovered by roentgenogram | Most involved |
| Metaphysial lesions | Mostly under form of enchondroses | Mostly under form of enchondroses | Secondarily under form of enchondroses |
| Laterality | Unilateral | Bilateral | Bilateral |
| Appearance at adult age | Probably rare | Rare | Frequent |
| Shortening of long bones | Great; essential character | Variable; secondary | Variable; secondary |
| X-ray picture | First soft and later all forms progress to ossification | | |
| Bones involved | Phalanges, upper extremity especially | Long bones | Long and small bones |
| Prognosis | Rapid growth; skin may ulcerate; growth may be excessive | Benign; may cause pressure on nerves, blood vessels, etc. | Progressive to end of period of growth |

Dyschondroplasia produces multiple lesions, most marked on the upper extremity, giving the appearance of periosteal origin. In some cases the growth has seemingly appeared on the site of an old injury, apparently developing from an islet of cartilage. The progress of the dyschondroplasia may be rapid, so much so that the patient may request amputation. Spontaneous fractures are common. When the inner surface of the ilium is involved, the growth may cause ulceration into the lower part of the bowel.

Chondromatosis is always hemiplegic. Fractures are common. Deformity from overgrowth and dislocation of joints also occurs. After the end of the period of growth, when further development of the chondromatosis has ceased, resection may be undertaken to correct the deformity of the overgrown bones.

RYAN, Vancouver, B. C.

HISTOLOGICAL OBSERVATIONS IN FIVE CASES OF CONGENITAL CRANIOTABES. T. BANG, J. Pediat. (Tokyo), no. 436, Sept. 20, 1936, p. 1297.

In the long bones (ulna and ribs) of five patients with congenital craniotabes slight atrophic changes at the diaphysial ends were noted, but a typical rachitic picture was not present. In sections made from the soft areas of the parietal bones of persons with typical congenital craniotabes Bang has found a definite decrease of osseous tissue and a widening of the interosseous spaces, in which are numerous capillaries. In the areas along the sagittal suture the osseous tissue lay in a single thin layer or even in scattered islands and finally was lost in the mass of connective tissue. The histologic evidence points strongly to an expansive growth of the membranous bone at the expense of growth in thickness. The defect appears to be in the apposition of the bones. In localized craniotabes the histologic picture indicates a defect of osseous tissue resulting from vascular resorption. Both forms, however, may be regarded as varieties of local osteoporosis.

KATO, Chicago.

FAMILIAL OSTEOPECILIA. J. RISSEEUW, Nederl. tijdschr. v. geneesk. **80**:3827 (Aug. 22) 1936.

Osteopecilia (spotted bones) in a father, six children and a grandchild is described. Three members of the family are free from the trouble; the others have

joint pains to varying degrees in their wrists and knees. One of the patients appears to have suffered from osteomyelitis of the tibia. A causal relation between this osteomyelitis and the osteopecilia is thought improbable. In two patients an exostosis was found.

VAN CREVELD, Amsterdam, Netherlands.

## Diseases of the Eye

CHOICE OF A SURGICAL PROCEDURE FOR STRABISMUS. H. G. MERRILL, Arch. Ophth. **16**:643 (Oct.) 1936.

It is recognized that many surgeons employ but one of the many procedures for the correction of strabismus. With this situation Merrill does not agree, feeling, as he does, that one operation cannot be ideal for all cases. He uses three procedures: In a case of extreme lateral deviation in which the area of temporary bulging caused by tucking would not be objectionable, tucking with partial tenotomy is done. In a similar case in which the area of bulging would be objectionable, an advancement is made, together with a tenotomy. For moderate deviations, the O'Connor cinch shortening is used, with recession of the opposing muscle.

WESCOTT, Chicago.

INHERITANCE OF OPAQUE NERVE FIBRES IN THE RETINA (PAPILLA LEPORINA). E. A. COCKAYNE, Brit. J. Ophth. **20**:569 (Oct.) 1936.

After describing the development of opaque nerve fibers and enumerating the various congenital anomalies which have been found associated with this condition, Cockayne gives the pedigree of a family in which ten members are affected: In four of them the condition is bilateral; in six, unilateral. In all of them the area covered by the opaque fibers is small. Five males and five females are affected, and in two of each sex the condition is bilateral. Of those examined in the sibships containing affected members, ten (five males and five females) are affected, and ten (four males and six females) are normal. Thus the ratio of affected to normal persons is 1:1, and descent is direct in every case. Males and females show the condition to an equal extent, and it is bilateral in the same number of females as of males. Both these observations are contrary to expectation if it is sex-linked. It is true that there is no instance of transmission of the abnormality by a male, but only one of the affected males has children, and only one of these children is old enough to show the defect.

Though the pedigree does not disprove Kisõ's hypothesis that the condition is sex-linked, its inheritance is quite in accord with that of autosomal dominants, and since autosomal dominants are common and sex-linked dominants are of extreme rarity in man it is probable that opaque nerve fibers fall into the former rather than into the latter group.

W. ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

CONGENITAL BLINDNESS;? BILATERAL PSEUDO-GLIOMA. D. PATERSON, Proc. Roy. Soc. Med. **29**:1433 (Sept.) 1936.

A boy aged 5 months was noticed to have a yellow opacity in the center of each eye when he was a few days old. One of the mother's sisters had two blind children, boys. One of these children had an eye removed, and the pathologic report was pseudoglioma. Both children died. Another cousin was also blind and died in infancy. One of the patient's uncles died at the age of 4 months and was blind.

The ophthalmologist suggested that the condition was one of double pseudoglioma, which he described as a fibrocicatricial exudate immediately behind the lenses, a part of gross uveitis.

WILLIAMSON, New Orleans.

THE ETIOLOGY OF FAMILIAL DISEASES OF THE OPTIC NERVE. A. RIFAT, Ann. d'ocul. **173**:702 (Sept.) 1936.

Subacute retrobulbar neuritis of Leber and familial, or total, atrophy of the optic nerve have an obscure etiology, and up to now it has not been possible to attribute these diseases to any precise cause. In the genesis of the familial disease the rôle of syphilis has recently been stressed by Leredde, who, because of the chronic character of syphilis, attributed to it a preponderant influence in the causation of familial atrophy of the optic nerve. It is also known that syphilis is the only hereditary and congenital disease that is transmitted to several generations. There exist in the literature some observations which suggest that Leber's disease might be considered a manifestation of hereditary syphilis. Buisson in his thesis of 1899 reported on a brother and a sister who presented the classic picture of this condition; five brothers and sisters died young, and two others were born dead. In these cases syphilis can only be suspected, but the evidence points strongly to the probability of its presence. In 1873 Schmidt-Rimpler reported cases of subacute retrobulbar neuritis in which pigmentary retinitis was observed.

Rifat recently examined a family in which there were six children living. Three presented, besides typical pigmentary retinitis, unquestionable signs of hereditary syphilis. The observations in seven cases are given in detail. He believes that familial disease of the optic nerve appears in three forms: The first is the subacute retrobulbar neuritis of Leber. In this condition the lesions affect only the macular branch of the optic nerve. The onset occurs usually around the age of from 20 to 30 years; the condition progresses for a year or two, then remains stationary and is never cured. The second form is familial atrophy of the optic nerve, which affects all the branches of the nerve. Absence of a central scotoma and peripheral shrinking of the visual field differentiate this condition from the disease of Leber. There is partial blindness, which rarely progresses to complete blindness, and this is associated with mental retardation. The third form is familial congenital atrophy of the optic nerve, a condition which exists at birth and usually involves several members of the same family in the same generation and in successive generations. Syphilis should be searched for in a systematic manner by all the methods at one's disposal in all cases of familial disease affecting vision. McKEE, Montreal, Canada. [ARCH. OPHTH.]

SURGICAL TREATMENT OF CONGENITAL COLOBOMA OF THE LIDS. J. CHARAMIS, Ann. d'ocul. **173**:810 (Oct.) 1936.

Congenital coloboma of the lids, a rare malformation, was first described by Mayer, in a thesis published from Montpellier in 1808. The first study to be published in England was that by Wylde in 1862, which was a more thorough study than that of Mayer. Interesting are the reports by von Hippel in 1907 and Pagenstecher in 1912. Among recent reports the writer cites that of van der Hoeve in 1921.

A general description of coloboma and the different theories to account for it are given. Charamis describes the case of a patient, a girl, whom he followed from birth. She was examined for the first time at the age of 6 months and again at the age of 9 years; no treatment had been carried out. The father had syphilis, and the child was given antisyphilitic treatment. There were no other congenital anomalies. The cornea was intact, although it was completely uncovered with the lids closed, so it was continually exposed and without protection. The coloboma occupied nearly the whole width of the upper lid and extended practically to the limits of the tarsus. However, the movements of the upper lid were conserved despite this.

As regards the etiology, Charamis thinks that syphilis should be taken into serious consideration. This accords with the theory of van Duyse. The treatment of all palpebral colobomas should be surgical. Sometimes a simple drawing

together of the border suffices; for those of greater width blepharoplastic operations are necessary. The correction in the case observed by Charamis is described in detail, and the article is illustrated with five photographs.

S. H. McKee, Montreal, Canada. [Arch. Ophth.]

Treatment of Trachoma in Children. M. Zachert, Rev. internat. du trachome **13**:177 (Oct.) 1936.

Trachoma in children is generally benign and is rarely associated with severe complications of the cornea or lid. Though children have less immunity to the contagion than adults, their resistance to its progress is greater. The granulations should be crushed individually and in several sittings. Frottage with chaulmoogra oil is well tolerated.

J. E. Lebensohn, Chicago. [Arch. Ophth.]

Heredity and Consanguinity in Ophthalmology. B. J. Tiscornia, Rev. méd. latino-am. **21**:1343 (Sept.) 1936.

Tiscornia gives a detailed résumé of the literature on heredity and consanguinity. In developing his theme he follows the evolution of laws of heredity among vegetables, animals and the human species. For human beings he discusses the abnormalities of the eye that can be transmitted by heredity and gives a table showing the conditions in patients at a clinic rich in ocular diseases. The bibliography is very complete.

Dwyer, Kansas City, Mo.

Hypodermic Injections of Carotene in the Treatment of Phlyctenular Conditions and Vitamin A Deficiency Diseases in Ophthalmology. M. C. Tai, Chinese M. J. **50**:1453 (Oct.) 1936.

Cod liver oil possesses an unpleasant smell and is difficult to preserve from oxidation. Eggs, milk and butter are sometimes not well digested by certain patients. Vegetables are seasonable products and, even when available, may cause gastro-intestinal upsets. Hypodermic administration of carotene in ampules obviates all the difficulties of oral ingestion. The only contraindication to its use is cirrhosis of the liver. Rigid asepsis should be observed in administering it, otherwise moderate dermatitis may develop. Carotene is inexpensive and is available in large amounts. It is produced in China and is easily obtained in that country and therefore may be widely used to great advantage in treating certain ocular conditions there.

S. H. McKee, Montreal, Canada. [Arch. Ophth.]

## Skin Diseases; Allergy

Study of the Prophylactic Action of an Extract of Poison Ivy in the Control of Rhus Dermatitis. J. M. Blank and A. F. Coca, J. Allergy **7**:552 (Sept.) 1936.

Much time was being lost in CCC Camp M C-64, Morristown, N. J., as a result of dermatitis caused by poison ivy and poison sumac. After trying other forms of medication and control it was decided to use an extract of ivy in oil in prophylaxis and in treatment.

In prophylaxis, group A was given four injections at weekly intervals of 0.5 cc. of almond oil containing 10 per cent by volume acetone and 0.1 per cent solids extracted from poison ivy leaves with acetone and freed from chlorophyll. Group B received four injections at weekly intervals of 1 cc. of a similar extract containing 0.66 per cent solids. Group C received no prophylactic injections.

As dermatitis occurred in the three groups the men were treated in rotation with (1) the stronger extract, (2) the weaker extract and (3) almond oil con-

taining 10 per cent acetone. Nine of the forty-five men comprising group A, three of the forty men in group B and thirty of the forty-five men in group C presented dermatitis. Six weeks from the start of this régime there were no more cases of dermatitis.

HOYER, Cincinnati.

USE OF BLISTER FLUID FOR PASSIVE TRANSFER SKIN TEST. S. J. PARLATO, J. Allergy **7**:573 (Sept.) 1936.

A girl known to be allergic received an accidental burn sufficiently severe to cause a blister. The fluid from the blister was injected into three places on the arm of each of two nonallergic persons. Twenty-four hours later these sites were tested with extracts of substances to which the allergic patient was sensitive; all the sites gave positive reactions; the controls were negative. The reagins in the sensitized sites could be exhausted with repeated injections of one of the extracts to which the patient was sensitive.

Blisters were produced on the thighs of the patient with a cantharides plaster. The fluid from the blisters and serum from blood withdrawn from the arm were injected into the arms of two nonallergic persons. The sites of the injections gave positive reactions when tested twenty-four hours later. This corroborates the work of Spain and Newell.

Parlato feels that blister fluid might be used for performing the Prausnitz-Küstner test in children from whom it is difficult to obtain blood.

HOYER, Cincinnati.

LIPOMA OF THE THUMB AND INDEX FINGER RESEMBLING ELEPHANTIASIS. B. REICH, Deutsche Ztschr. f. Chir. **247**:555 (Sept. 23) 1936.

This condition occurred in a girl 12 years of age. During the patient's first year of life the mother observed a swelling of the right thumb and index finger, which gradually increased as the child grew older. The mass was of moderate and uniform density and caused no disability except that incident to its size. The skin over the mass was normal, and a roentgenogram showed no bony abnormality. The preoperative diagnosis was uncertain, but a primary local disturbance of growth of the same nature as macroglossia, for example, or a lymphangioma were considered most likely. On operation a well delimited lipoma was removed. The article is well illustrated. Lipoma of a digit is apparently uncommon.

GLASER, Rochester, N. Y.

DIETARY THERAPY FOR PSORIASIS IN CHILDREN. E. SCHIFF, Jahrb. f. Kinderh. **145**:299 (Nov.) 1935.

A 5 year old child with psoriasis in a severe form was successfully treated by means of a fat-free diet. This diet consisted of fresh fruit, fresh raw vegetables, and orange, tomato and carrot juices in small quantities. Cevitamic acid in the form of tablets was given orally regularly, and at one time cevitamic acid was given intravenously.

LANDAU, Hannibal, Mo.

FURTHER OBSERVATIONS ON FOOD ALLERGY IN ASSOCIATION WITH INFANTILE ECZEMA. P. GYÖRGY, E. MORO and E. WITEBSKY, Klin. Wchnschr. **11**:1172 (July 9) 1932.

The cutaneous reaction to egg white is observed to occur with particular frequency in infants with eczema. The clinical concept of eczema may vary in different clinics. In 68 per cent of one hundred and ninety-three cases of eczema in the university clinic at Heidelberg allergic reactions were shown. The cutaneous as distinguished from the intracutaneous reaction is even more distinctive of sensitivity to egg white than its frequency and is associated with the presence of specific antibodies in the blood, which can be elicited by means of the Prausnitz-

Küstner passive transfer test. While similar allergy can be shown with the passive transfer test with cow's milk, the cutaneous reaction to milk is seldom positive. There is, however, a close parallelism between the Prausnitz-Küstner and the intracutaneous reaction in the case of milk allergy. Positive results have been obtained with flour exclusively in some instances, and with potato and veal in one case each. Sensitivity to veal appears to be associated with milk allergy.

SILVERMAN, Syracuse, N. Y.

TREATMENT OF IMPETIGO CONTAGIOSA IN CHILDHOOD. F. OXENIUS, München. med. Wchnschr. **82**:584 (April 11) 1935.

Crusts are removed with absorbent cotton soaked in hydrogen peroxide. Tincture of iodine and later 1 per cent phenylethylhydantoin and paste of zinc oxide are applied to the lesions. The lesions are carefully covered with suitable dressings to prevent the spread of the infection and to keep the medicament in place. Oxenius also uses sulfur baths of ten mnutes' duration, after which the lesions are again carefully covered. The same treatment is used for pemphigus neonatorum except that potassium permanganate baths are used.

BRAHDY, Mount Vernon, N. Y.

ENDEMIC OUTBREAK OF A SKIN DISEASE CAUSED BY BITES OF AEDES CINEREUS. H. K. F. COHEN, Nederl. tijdschr. v. geneesk. **80**:4200 (Sept. 19) 1936.

Cohen records an endemic outbreak and one isolated case of a skin disease localized especially around the ankles. The picture simulated erythema nodosum, erysipelas multiforme and ulcus cruris simplex. The cause proved to be the bites of gnats of the species Aedes cinereus, which can suddenly appear in large numbers at the end of June and the beginning of July.

VAN CREVELD, Amsterdam, Netherlands.

ENDEMIC OCCURRENCE OF WARTS. R. D. G. P. SIMONS, Nederl. tijdschr. v. geneesk. **80**:4308 (Sept. 26) 1936.

Simons gives a description of an endemic of warts (twenty-three cases) in an institution for idiots. Of the twenty-three patients, only nine had shown the condition one year before. The ages of the patients, all of whom impressed one as infantile, ranged from 12 to 30 years.

VAN CREVELD, Amsterdam, Netherlands.

## Surgery and Orthopedics

SPINAL ANESTHESIA FOR POOR PEDIATRIC SURGICAL RISKS. J. L. AMSTER, M. Rec. **144**:213 (Sept. 2) 1936.

Amster summarizes the literature on spinal anesthesia in children from 1900 to 1922. He gives a few details in the management of the child before the anesthetic is used and recommends the Labat technic. He discusses the results obtained in fifty-three children who presented poor operative risks, the manner in which the anesthetic was administered, the drugs employed in each case and the resuscitative measures employed when accidents and fatalities occurred. In conclusion, he points out the advantages of spinal anesthesia.

WILLIAMSON, New Orleans.

TIME CHANGES IN THE RELATIVE MORTALITY FROM ACCIDENTAL BURNS AMONG CHILDREN IN DIFFERENT GEOGRAPHIC REGIONS OF THE UNITED STATES, 1925-1932. W. M. GAFAFER, Pub. Health Rep. **51**:1308 (Sept. 13) 1936.

In general, the number of deaths from accidental burns has been decreasing for the last eight years. Seventy per cent of all deaths from burns in children

under 15 years of age were in children under 5 years of age. In all regions, the greatest number of deaths was in the group below the age of 2, except the southeastern region, where it was in the 3 year group. The decrease in mortality was southeastern, northeastern, north central and western, in that order.

SANFORD, Chicago.

CHILDREN'S SURGICAL CLINIC. L. OMBRÉDANNE, Progrès méd., Sept. 12, 1936, p. 1421.

The patients shown by Professor Ombrédanne were two infants with harelip, one boy 3 years old with congenital pseudarthrosis of the tibia and fibula, one child with torticollis, the condition being presented as due to spasma of the sternocleidomastoid muscle following a mastoid operation, and one child with tuberculous cervical adenitis. The advisability and the types of surgical intervention in such cases are discussed. One wonders, in view of the recent understanding of atlanto-axial dislocation, whether the case presented as one of spasmodic torticollis might not be of that nature.

LESLIE, Evanston, Ill.

BILATERAL "MARCH FOOT." SAVÉS, Rev. d'orthop. **23**:529 (Sept.) 1936.

"March foot" is usually considered to be unilateral. The case reported is interesting as refuting the hypothesis that it is always so.

RYAN, Vancouver, B. C.

SPECIAL TREATMENT OF BILATERAL PARALYSIS OF THE HIP MUSCLES. C. SCHAAP, Rev. d'orthop. **23**:534 (Sept.) 1936.

Any mechanical appliance used in the treatment of paralysis of the muscles controlling the movements of the thigh on the pelvis must meet three conditions: (*a*) It must permit sitting; (*b*) it must be sufficiently strong to retain the upright position of the body in standing or walking, and (*c*) it must permit easy walking.

Schaap refers to the appliance developed by Mommsen for use in the treatment of paralysis of the gluteus maximus. Schaap has incorporated this appliance, the *physiologisches Hüftstreckfeder,* into a body and leg corset to permit its use in the treatment of bilateral paralysis of the extensors of the thigh. From the description given, this appliance may be well worth developing further.

RYAN, Vancouver, B. C.

## Miscellaneous

EFFECT OF OXYGEN INHALATION ON THE COURSE OF ACUTE ALCOHOLIC INTOXICATION. T. C. BUTLER, J. Pharmacol. & Exper. Therap. **58**:68 (Sept.) 1936.

Butler questions the validity of certain work on animals and man showing that inhalation of oxygen lessened the effects of alcohol, at times saving life in rabbits after lethal doses.

"A priori it would scarcely be expected that the inhalation of oxygen should influence the course of alcoholic intoxication, first, because it is difficult to accept the view that alcohol exerts its narcotic action in the central nervous system by interfering with cellular oxidation, and, second, because there is no ready explanation of how the small extra amount of oxygen in the arterial blood could influence tissue oxidation."

He therefore investigated the effects of oxygen on a considerable number of animals and found that oxygen was not antidotal to alcohol given in lethal doses to mice, that it did not materially change the behavior of guinea-pigs and rabbits which had received small doses of alcohol, and that it did not restore certain reflexes abolished in rabbits by alcohol.

PILCHER, Cleveland.

THE RÔLE OF THE PHYSICIAN IN VOCATIONAL GUIDANCE. G. HEUYER, Rev. méd.-sociale de l'enf. **5**:331 (Sept.-Oct.) 1936.

The doctor should know what physical qualities are suitable for good work in certain trades and the methods available for determining the possession of such qualities. Vocational guidance must fit such different groups as children finishing primary school, boys and girls finishing secondary school, physically or mentally abnormal children and delinquent children.

BROWNE, Detroit.

THE INTERNAL SECRETION OF THE EMBRYONIC TISSUES: ITS BIOLOGICAL SIGNIFICANCE AND ITS IMPORTANCE IN PRACTICAL MEDICINE. N. E. ISCHLONDSKY, J. Egyptian M. A. **19**:306 (June) 1936.

This article represents three lectures delivered by Ischlondsky before the Egyptian Medical Association at Cairo on March 7, 14 and 16, 1936. One abstracts the article with temerity. Dr. Ischlondsky's work is so revolutionary that one is inclined to view it with skepticism. Yet his argumentation and explanation are so lucid, so reasonable that one cannot but feel he has perhaps hit on something. The lectures when printed occupy some 120 pages. They tell of an embryonic tissue extract the development of which was quite fortuitous. After the extract had been applied in senile and sick animals with brilliant results, it was tried in human beings with similar effectiveness. It was used in all sorts of conditions: dementia praecox, arteriosclerosis, cataract, diabetes insipidus, tuberculosis and migraine, among others. The clinical histories of the cases cited are included. The last lecture is an explanation of the seemingly contradictory effects and a convincing argument in defense of the tabooed problem of regenerescence. The bibliography is not long and is chiefly of the author's own work. It suffices to state that the abstractor intends to read more on this most interesting work.

MULHERIN, Augusta, Ga.

# Society Transactions

## AMERICAN PEDIATRIC SOCIETY

*Hot Springs, Va., April 29-May 1, 1937*

HENRY F. HELMHOLZ, M.D., *President*

HUGH MCCULLOCH, M.D., *Secretary*

*(Continued from page 196)*

### Third Session

*Friday Morning, April 30*

STUDIES OF FETAL RESPIRATORY MOVEMENTS: II. RECORDING METHODS. DR. BARNET E. BONAR and DR. CON FENNING (by invitation), Salt Lake City.

This article will appear in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

TONIC CERVICAL REFLEXES IN CHILDREN CONSIDERED FROM THE PROGNOSTIC POINT OF VIEW. DR. RANDOLPH K. BYERS (by invitation), Boston.

This article will be published in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

CARDIAC COMPLICATIONS IN ACUTE HEMORRHAGIC NEPHRITIS. DR. MITCHELL I. RUBIN (by invitation) and DR. MILTON RAPOPORT (by invitation), Philadelphia.

This article will appear in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

ENDARTERITIS OBLITERANS IN AN INFANT GIRL. DR. DEWITT H. SHERMAN, DR. KORNEL TERPLAN (by invitation) and DR. J. SUTTON REGAN (by invitation), Buffalo.

A baby aged 1 year, of Italian extraction, was admitted because of gangrene of the two distal phalanges of the little finger of the right hand, which manifested itself definitely at the age of 10 months. The family history was not relative. The general physical condition was fair. The child was supposed to have had pneumonia at 6 months; she also had a doubtful history of a previous mild infection accompanied by a temporary cutaneous rash. Virtually from birth, her cheeks were periodically more or less cyanotic. At 3 weeks of age she had periods every two or three days of swelling and redness of the index and third fingers of the left hand, which persisted one day. Later these fingers became cyanotic, remained so for twenty-four hours and then returned to the normal color, never pale.

On admission her radial, ulnar and tibial arteries were easily palpable but the ends of most of her fingers were somewhat swollen and at intervals cyanotic. Dry gangrene involved the two distal phalanges of the right little finger, and dark spots were evident on the tips of the ring finger and little finger of the left hand, with trophic changes of the finger-nails.

Periarteritis nodosa was eliminated by (*a*) careful study of the ateries, (*b*) arteriographic examination and (*c*) histologic studies. An early study was made

of the temperature of the skin. There was no change (*a*) under application of ether, (*b*) injection of procaine hydrochloride into the ulnar nerve or (*c*) crushing of the nerve. These procedures eliminated Raynaud's disease as an important factor.

Later, arteriography with thorium dioxide was successfully carried out. The capillaries in the skin of the fingers seemed to show a structural defect.

After a brief vacation at home the child presented the left arm swollen, red and painful. At the same time the cheeks became redder and more cyanotic than formerly, and dry gangrene developed in the distal phalanges of the fingers of the left hand. All the fingers that became gangrenous were self-amputated. Early she responded with a 4 plus reaction to an intradermal tuberculin test, but after desensitization she showed a negative reaction and has continued to do so. Roentgen examination of the chest revealed an old interlobar pleuritis with an increase in the size and density of the shadow at the hilus. Further x-ray pictures of the bones or of the spine disclosed only normal conditions. Complete studies of the blood showed anemia but nothing abnormal as regards coagulation and bleeding time, viscosity, fragility, Wassermann or Kahn reaction, bacterial content and chemical composition.

*Histologic Report by Dr. Terplan.*—A finger amputated at the third phalanx, 2 cm. in length, was examined. The distal phalanx showed greenish-black dry gangrene over a distance of 0.5 cm. The nail was completely destroyed. Sections were taken from different parts of the second phalanx, which appeared distinctly inflamed, apparently reactive to the distal gangrene.

The histologic picture revealed completely obliterating endarteritis especially in the dorsal artery. The elastic layer was well preserved. The lumen was replaced by an organizing tissue, which included a few small capillaries containing erythrocytes. In addition, there was hemosiderin pigment in a few histiocytes within the obliterated lumen. The media also was well preserved and, especially in the smaller arteries, rather thickened. The adventitial wall was distinctly thickened and contained many newly formed capillaries. The media and adventitia showed signs of recent inflammation, which apparently was a part of the diffuse reactive process in the amputated gangrenous phalanges. The diagnosis was: endarteritis obliterans with cause unknown except that it was possibly due to a structural defect.

DISCUSSION

DR. HUGH MCCULLOCH, St. Louis: I have had the privilege and pleasure of seeing Dr. Sherman's report before. It is quite interesting to speculate as to the etiology of the lesion. He has apparently ruled out the usual causes of vascular occlusion in postnatal life. It occurs to me that the lesion might be a congenital one in the intima or subintimal layers of the arteries in the fingers, which was not complete enough to make the circulation inadequate during the first months of life but which rendered the circulation inadequate as the hand was used more. Changes of this sort may occur elsewhere in the body. The lesion may be similar to the atresia of muscle fibers seen in the gastro-intestinal tract, occasionally in heart muscle and probably other parts. Calcifying endarteritis obliterans of the myocardium has been reported in children under the age of 2. The child may live for some time because the anastomoses in the affected parts, in this case in the finger, allow nutrition to be maintained for a certain length of time, thereby preventing gangrene.

DR. DEWITT H. SHERMAN, Buffalo: There are one or two points I should like to stress, and I should like to mention an unusual procedure.

The first point is that the arteriogram must be snapped during the first two or three pulsations after the opaque substance is injected into the artery. Unless the arteriogram is taken that promptly, the opaque substance will have passed along into the veins and will hence give the mistaken diagnosis periarteritis nodosa.

Our pathologist, Dr. Kornel Terplan, is not in sympathy with the suggestion that a congenital defect of the terminal capillaries in an infant might be a dominant cause of endarteritis obliterans.

Having secured no benefit from treatment with fever, either malarial or typhoid, or from the pavex, used daily for months, or from any other methods or medicaments usually tried, I was persuaded to try local hypodermic injection of oxygen by Dr. John H. Evans, our most prominent anesthetist, head of the department of anesthetics in the medical school of the University of Buffalo and a member of the staff of the Buffalo General Hospital and also the Children's Hospital.

To evolve a rational explanation of how oxygen injected hypodermically may be efficient in endarteritis obliterans is rather difficult, unless the injected gas possibly renders some protein base unfavorable to the presence or the growth of an undiscovered germ or virus. Though this idea seemed wild, there was no danger if the injection was properly given. We tried the injection of oxygen, since Dr. Evans himself injected the oxygen daily into the forearms without trouble and gently worked it down into the finger-tips. The change in color from that of a decided cyanosis to a rather brilliant redness was remarkable, and this change persisted for from eighteen to twenty hours, which was from six to eight hours longer than the best change in color produced after a treatment with the positive and negative pressure apparatus.

This hypodermic injection of oxygen failed to produce any permanent or restraining results. It should also be noted that the injections of oxygen were more easily tolerated than the treatment by the pavex. In justification of such an experimental treatment I must, in fairness to Dr. Evans, state that he has secured magical results from injections of oxygen near many chronic lesions of the skin.

COAGULATION OF THE BLOOD IN ANAPHYLACTIC AND OTHER TYPES OF SHOCK. DR. CHARLES F. MCKHANN and ISRAEL KAPNICK, A.B. (by invitation), Boston.

The product of coagulation of blood, the clot, is thought of as deriving its character from fibrin, yet the water-holding capacity and retractility of the clot have been found not to depend primarily on the level of the blood fibrinogen.

Tissue extract and platelets enter together with fibrinogen into the formation of the clot, so that the determination of fibrin as usually carried out measures the combination of fibrinogen, platelets and tissue extract. Yet there is no definite evidence that platelets and tissue protein go into the clot quantitatively. Rather it appears that the level of the blood platelets determines to some extent the amount of tissue protein which enters the clot combination.

It seems that the platelets influence retraction and that the tissue extract influences hydration, but that the presence of the latter in excessive amounts, especially in the absence of platelets, results in the loss of the hydrating capacity and the suppression of true clotting.

These experiments indicated that the rate of coagulation and the type of clot may be in part a function of the quantitative relationship of the fibrinogen, the tissue extract and the blood platelets (number and volume).

The yield of fibrin from a sample of blood is increased in many acute and chronic illnesses in which injury or destruction of tissues occurs. An indirect evidence that tissue proteins may give rise to this increase is found in the lessened rate of retraction in clots in febrile diseases even in the presence of a normal number and volume of platelets. It has been earlier pointed out that lessening of the retractility of clots appears to depend on the ratio of tissue protein to platelets. Reduction of platelets is not essential for diminution in retractility if the level of the tissue protein is elevated.

Because it had proved possible in the test tube to produce at will alterations in the coagulation time and in the character of blood clots by varying the relationship of platelets, tissue extract and fibrinogen, it seemed desirable to investigate experimentally the effects of similar variation in the animal. The effects of intraperitoneal and intravenous injection of tissue protein into rabbits have been studied. Intraperitoneal injection of small doses of tissue protein led to shortening in the coagulation time of the blood. Although the platelet count remained normal, the clots usually showed firm consistency and diminished retractility, presumed to be due to the hydrating effect of the inclusion of some of the injected

tissue extract. The yield of fibrin was found to be slightly increased. When larger amounts of tissue extract were given intraperitoneally, the blood coagulation time was also shortened, the hydrophilic character of the clot was still more apparent, but the platelet count of the animal dropped sharply.

Intravenous injection of small amounts of undiluted tissue extract resulted promptly in death from intravascular coagulation with the formation of dense clots in the right side of the heart and in the lungs. Blood taken after death was incoagulable and showed a very low platelet level as well as a decrease in fibrinogen. Larger doses could be given intravenously without death of the animal if administered in high dilution and slowly. The blood, however, was rendered similarly incoagulable. The platelet and fibrinogen levels fell sharply. The reaction which culminated in death represented a type of shock of uniform symptomatology resembling strikingly in certain features fatal anaphylactic shock.

It has long been known that in anaphylactic as well as in arsphenamine and peptone shock the blood is rendered incoagulable, whereas in burn shock the coagulability of the blood is usually increased and there is a marked hydrophilic character to the clot. As early as 1915, a drop in blood platelets had been noted in various types of shock.

In vitro, the addition of tissue extract to samples of blood greatly hastened coagulation and rendered the clot more hydrophilic, but in the presence of a diminution in blood platelets precipitation of the fibrinogen occurred, and no true clot resulted. In vivo, tissue extract administered intraperitoneally acted as it did in small amounts in the test tube, while intravenous injections of the extract resulted in deplateletization and suppression of clotting. The similarity to the response of the allergic patient to the injection of tissue protein is accentuated when the effects of local allergy, mild general allergy and anaphylaxis are considered. A local allergic reaction produced increased coagulability of the capillary blood. Mild general allergic responses likewise were usually associated with increased coagulability but might pass gradually to the allergic types of purpura, while anaphylaxis produced deplateletization and incoagulability of the blood.

It seems that a physiologic mechanism defends against the effects of tissue extracts in the vascular system; perhaps this is a defense against intravascular coagulation. The response is characterized by a drop in platelets and in fibrinogen. Thus the opposing types of effect of tissue extract in blood coagulation may be explained: A positive effect in shortening coagulation time and in improving the hemostatic qualities of the clot is produced when tissue extract is applied locally or is introduced into the intercellular spaces whence it may slowly enter the circulation; a drastic negative effect, rendering the blood incoagulable, occurs when the material enters the blood stream directly.

While we cannot say definitely that allergic shock, burn shock and shock associated with acute infection are due to the release of protein substances from the tissues into the intercellular spaces and subsequently into the blood stream, we can point out that the alterations in rate of coagulation and type of blood clot in these cases might be accounted for on such a basis.

### DISCUSSION

DR. A. A. WEECH, New York: I should like to ask whether Dr. McKhann has any idea as to the route by which this protein gets into the circulation. Does histamine shock bring about the same kind of event?

DR. CHARLES F. MCKHANN, Boston: It seems to us an interesting hypothesis that tissue protein may go back and forth between the tissues and the circulation. There is a good deal of biochemical and physiologic evidence that it does, but the actual mechanism we do not know.

Histamine shock differs considerably from shock produced by tissue protein.

The study of heparin is decidedly in a preliminary stage; there seems to be a more or less quantitative relationship, so one has to gage accurately the amount of heparin used. If the amount of heparin is inadequate, the process goes along as though none had been given; if the heparin is more than adequate, there is no reaction. Further work must be done in a quantitative manner before there is any clinical application from this work.

POSSIBILITY OF SENSITIZATION TO TUBERCULIN. DR. WALDO E. NELSON (by invitation), Cincinnati.

An attempt has been made to determine whether tuberculin injected intracutaneously may sensitize the nontuberculous host.

My co-workers and I have performed repeated tuberculin tests over a period of two years on groups of children who had no reaction to two initial tests with the first and second testing strengths of purified protein derivative. Various tuberculins were employed in the series of repeated tests in separate subgroups. A number of positive reactions were obtained in each of the subgroups in every test subsequent to the two initial tests. There was no consistency, however, in the responses indicative of induced sensitization in the individual child in successive tests. These groups, which had been receiving repeated injections of tuberculin over a period of two years, gave the same responses with the second testing strengths of purified protein derivative and old tuberculin as a group of children not previously tested except for initial negative tests forty-eight hours earlier with the first testing strengths of purified protein derivative and old tuberculin. Repeated tuberculin tests with purified protein derivatives and old tuberculin have also been performed in several other institutions, with similar results. Roentgenologic examination of a number of children who had positive reactions in one or more of the series of tests or whose reactions to all tests were negative revealed that a considerable percentage of them had evidence of calcification of a type which ordinarily is interpreted as tuberculous. Furthermore, in three different institutions the number of positive reactions to repeated tests was geater among the older children than among the younger ones. When measurements of the reactions were made at twenty-four as well as at forty-eight hours, it was found rather consistently that the weaker reactions were larger at twenty-four hours than at forty-eight hours and not infrequently the twenty-four hour reaction had faded entirely at the time of the latter reading. It has been suggested by others that this accelerated response may be evidence of tuberculin-induced sensitivity. Since we have observed this type of response in the first test with tuberculin and frequently in the second test (the first test with a large dose of tuberculin), at an interval of only forty-eight hours, we are inclined to doubt this hypothesis. Whether this is a specific or a nonspecific response is not clear. From our data, however, it seems not unlikely that it may be evidence of low tuberculous allergy resulting from a very minimal infection or of the waning of allergy of a previously higher degree.

Within the limits of the amounts of tuberculin injected in the various tests of this study, there appears to be no evidence that sensitivity to tuberculin is induced by injection of tuberculin in man. This does not imply that sensitization to tuberculin or to tuberculoprotein is impossible but that such sensitization probably does not result from the ordinary use of tuberculin for skin-testing purposes.

DISCUSSION

DR. BÉLA SCHICK, New York: The question discussed by Dr. Nelson is an old one. It has always been puzzling that tuberculin sensitization cannot be accomplished by injection of tuberculin. Even unheated tuberculin does not sensitize. Living and dead bacilli are necessary.

Quickly disappearing reactions of the sort which Dr. Nelson reports are in my experience pseudoreactions and not tuberculin reactions. It is important to know that intradermal testing with tuberculin, particularly that with large doses, may lead to erroneous diagnosis of tuberculosis on account of pseudoreactions. I believe that all Mantoux reactions or intracutaneous reactions with a diameter up to 10 and even to 15 mm. are questionable, especially if they disappear after forty-eight hours. A really positive intradermal test lasts much longer.

The knowledge of the existence of the pseudoreaction in intradermal testing with tuberculin is very important.

DR. CHARLES HENDEE SMITH, New York: I am not sure whether there was mention of the sites of these tests. It has been known for a long time that it is

possible to sensitize local areas of the skin. I cited an example of this in a paper read several years ago before this society. By mistake, repeated tests were made in the same area with increasing doses. Finally a strong reaction resulted, but by testing other areas of the skin the reaction was found an entirely negative one with the same dose. At autopsy no trace of tuberculosis was found.

It must be remembered that the skin can also be sensitized in the direction of lymphatic drainage. If one makes a tuberculin test in the lower part of the forearm and later another farther up, a tremendously enhanced reaction and sometimes reddening along the lymphatics may result. Any repeated tests should be done in new areas of the skin and in a direction opposite to that of the lymphatic drainage, or false positive reactions may result.

If patients can be sensitized to tuberculin, why is it that children tested every week over a long period, which in certain hospitals is the routine in all cases of negative reaction, do not react to later tests?

In my experience the only positive reactions on retesting are in persons whose sensitivity has been lowered, owing to fever or to overwhelming infections or in children who have contracted tuberculosis in the hospital.

I should like to ask what the doses were for the patients showing definite calcification not only in the lung fields but in the bronchopulmonary nodes. Was the dose run up for those patients or kept at a constantly low level? I think no patient should be considered as having a negative reaction to tuberculin unless there is a negative reaction to from 0.5 to 1 mg. of tuberculin. In tests done with as little as 0.001 mg. or its equivalent, variability is to be expected.

Dr. A. Graeme Mitchell, Cincinnati: Knowing the care with which Dr. Nelson has done this work and analyzed the results, there is little I can do except to emphasize one or two points. First, the point that the reaction to tuberculin may become negative under the influence of nonspecific factors. For example, in any febrile condition a positive reactor becomes negative sufficiently often so that this is significant. Therefore, if tuberculin tests are performed on admission of patients to the hospital, as a routine, a certain number of children who are acutely ill will have negative reactions, but if these tests were performed later, their reactions would be positive. Secondly, it is perhaps not widely known that certain types of minimal tuberculosis in the chest may be accompanied by a negative skin response to tuberculin. Apparently not infrequently, when there is present only the initial Ghon tubercle, which has become calcified, and calcification exists in the glands at the hilus, a positive reaction will not be found. Thirdly, there should be mentioned the variability of reaction in the same patient from time to time. Fourthly, it appears to me that the evidence is acceptable that even repeated injections of tuberculin do not cause sensitivity in the patient to the point that a positive skin reaction will occur. It would certainly be a disconcerting fact if this were the case, because one would never know how to interpret a reaction to tuberculin once the material had been injected.

Dr. Waldo E. Nelson, Cincinnati: I should like to thank these gentlemen for their discussion. In answer to Dr. Schick's question, there appears to be evidence that experimental animals can be sensitized with large quantities of nonheated tuberculin, the so-called M.A. 100 and the precipitated tuberculin (T.P.T.) of Seibert. This has been demonstrated by both Seibert and Sabin.

As far as pseudoreactions are concerned, I agree that some of the reactions may be nonspecific. For example, in an institution for foundlings simultaneous injections were performed with first and second testing strengths of old tuberculin and first and second strengths of purified protein derivative on the same group of infants, ranging in age from a few days to a few months. In practically all of these infants there was some reaction at twenty-four hours. In no instance was the area of induration of the reaction at forty-eight hours as large as 5 mm. in diameter, although there were several as large as 4 mm. Some of the reactions at twenty-four hours were as large as 15 mm. Because of the early age of these subjects and the consistency with which reactions were obtained and because similar results were obtained in another group of new-born infants, we are

inclined to wonder whether reactions as large as from 40 to 50 mm. at twenty-four hours with marked fading at forty-eight hours may not be evidence of low or waning allergy to the tubercle bacillus. This appears to be a possibility in view of the frequency of the observation of calcified lesions in association with such reactions.

In regard to the possibility of induced sensitization to the bouillon of the culture mediums, this may be a possibility for certain batches of old tuberculin but should not be so for purified protein derivative, M.A. 100 and T.P.T.

In answer to Dr. Smith's question regarding the sites of injection, in all but the second group the sites were varied. Some of the tests were performed on the legs, and responses of the same type were obtained. In the second group we purposely employed the forearms in all tests, alternating the forearms for the tests.

The amounts of tuberculin employed never exceeded 0.005 mg. of purified protein derivative or 1 part of old tuberculin in 100 parts of the diluent.

SENSITIVITY TO COW'S MILK IN INFANTS WITH ECZEMA. DR. LEWIS WEBB HILL, Boston.

Of 126 infants with eczema, in 104 the eczema began under the age of 6 months; in 52, under the age of 3 months. Most of the infants were eating nothing but cow's milk. Of 153 tested by the scratch method with cow's milk proteins, only 17 per cent gave positive reactions, but in another series of 64, who had all given negative reactions in scratch tests, 56 per cent showed reactions in positive intracutaneous tests. In most of these patients cow's milk was found to be an etiologic factor. Entire withdrawal of milk from the diet was found to be more effective in treatment than the use of heated milk or goat's milk. The sensitivity is usually of a low degree, and there are all variations, from the normal specific sensitivity of the skin shown by many infants who ingest cow's milk for the first time up to the more severe sensitivity in which the infant may be made violently ill by even small amounts of milk.

In a series of 50 normal infants, intracutaneous tests to milk were positive in 10 per cent.

Other phases of the subject discussed in this paper are: the development of sensitivity to milk; the etiologic significance of intracutaneous tests; the significance of infantile eczema as a phase in the development of immunity; heated milks, goat's milk and milk-free diets in therapy; the importance of sensitivity to casein in determining which of those methods to use; the effect of heat on the antigenic power of casein and of lactalbumin; the similarity of goat milk and cow milk casein; the normal and the abnormal antigenic response to foreign protein.

DISCUSSION

DR. FRANK C. NEFF, Kansas City, Mo.: I should like to ask Dr. Hill whether he has had any reaction by the intracutaneous route.

DR. L. EMMETT HOLT JR., Baltimore: I should like to ask whether the author has done any work on passive transfer of the sensitivity in these cases.

DR. LEWIS WEBB HILL, Boston: I have never had a general reaction with an intradermal test because I never do an intradermal test on a baby until the scratch test has been done, unless the baby has been eating the food all the time. If the baby has been eating cow's milk for three or four months, one knows that he is not very sensitive to it and that an intracutaneous test will do no harm.

In answer to the question concerning passive transfer of sensitivity, in this particular series I have attempted passive transfer of sensitivity to milk in eight cases; in four the results were positive, and in four, negative.

"AUTO PASSIVE TRANSFER." DR. D. MURRAY COWIE, Ann Arbor, Mich.

"Auto passive transfer" refers to the injection of the patient's own serum into his own skin where the allergic antibodies sojourn passively for several days. The

paper takes up such topics as: the immediate effect of the serum transfer to the skin; the specific intradermal reactions that develop in the areas of "auto passive transfer" as compared with those developing in the Prausnitz-Küstner passive transfer areas; the enhancement of the ordinary intradermal reaction by passive transfer and "auto passive transfer"; the method of study of the three component factors of an allergic reaction; the titration or assay of circulating passively sensitizing antibody.

DISCUSSION

DR. A. A. WEECH, New York: I should like to ask what technic was followed in testing for passive transfer.

DR. D. M. COWIE, Ann Arbor, Mich.: Blood is taken from the patient, the serum separated and 0.03 cc. injected intradermally into his skin in as many sites as desired. Frequently an immediate reaction occurs, which cannot be differentiated morphologically from an ordinary intradermal allergic reaction. This soon disappears. The nature of this reaction is not entirely clear; it occurs with the ordinary method of passive transfer as well. Twenty-four hours after the serum is injected, 0.03 cc. of the standard allergen under investigation is injected intradermally into the area of "auto passive transfer." If specific antibody is present in the serum, a typical intradermal reaction develops. Control tests on untreated skin are also run.

The antibody-antigen mixtures illustrated are investigated by their passive transfer to a nonallergic person's skin. If the antibody has been completely inactivated by the antigen and incubation, no reaction will occur in the area of passive transfer when standard antigen is injected into it.

*(To be continued)*

# Book Reviews

**Management of Obstetric Difficulties.** By Paul Titus, M.D. Price, $8.50. Pp. 879, with 314 illustrations. St. Louis: C. V. Mosby Company, 1937.

The past year has brought forth a number of new obstetric texts. Four textbooks on the general subject of obstetrics and one monograph on abortion have appeared in America, and now comes Titus' book on the "Management of Obstetric Difficulties." The complications and problems of pregnancy, labor and the puerperium are included. The book opens with a discussion of sterility. The causes of sterility and the methods of investigation are well given. All the voluminous literature on this subject cannot be reviewed in a handbook of this size, but an excellent discussion is given from which the student or the practitioner may derive much information. Methods of treatment are well presented. In the illustration depicting the treatment of endocervicitis by cautery, the cautery point shown is the heavy Paquelin type rather than the fine platinum wire loop favored by most gynecologists.

The diagnosis of pregnancy is well handled, and the chapter on the minor complications of pregnancy will be of considerable assistance to practitioners who include obstetrics in their professional activities. The chapter on surgical complications is sane and wise. The use of the noun "council" on page 156 instead of the verb "counsel" is probably chargeable to the proofreader.

Medical complications and diseases of the ovum, embryo and fetus occupy two chapters. In dealing with the latter the author makes no attempt to enter into an extended discussion, but he gives sufficient information to aid the practitioner materially.

The toxemia of pregnancy receives an adequate presentation. The author and his associates have contributed to the literature of this subject, and their views find expression in the discussion of the treatment. While obstetric opinion is not unanimous as to the rôle of hypoglycemia in late toxemia, the management is well handled here and the emphasis placed on the conservative treatment of severe late toxemia is in accord with the best obstetric thought of today. The conservative mind of the author is apparent also in the chapter on abortion and premature labor. Ectopic pregnancy is dealt with in a manner which will find favor with American obstetricians. Particularly to be commended is the rejection of the waiting policy formerly advocated by a few writers in the management of patients in whom serious bleeding has occurred.

The author meets a difficulty encountered by all writers of obstetric texts when he attacks the subject of contracted pelvis, the lack of an entirely satisfactory classification of pelvic abnormalities. Recent work is alluded to, and the present status of roentgenoscopic pelvic mensuration is outlined. The treatment is sane. Renewed emphasis is needed in this country on the fact that operative intervention is not invariably required and that mature clinical judgment may often make possible excellent results with conservative methods. It is refreshing to find in the section on hemorrhages the advice that packing for relief of postpartum bleeding is best done before dangerous loss of blood has occurred.

As to the comparative value of median and mediolateral episiotomy, opinions vary, as do the ideas of different men as to whether the incision should be made before the perineum is distended, with some possible muscular separation, or after stretching has indicated the probability of injury and its extent.

Therapeutic abortion and the induction of labor are clearly explained. One may not subscribe wholly to the statement that overlapping of the parietal bones as shown by roentgenogram is a clear indication of intra-uterine fetal death. It is true that in the great majority of cases it is, but at least one investigator has shown that overlapping may be demonstrated roentgenographically in the engaged head in an infant subsequently born alive. These chapters as a whole are good. The reviewer subscribes to the author's low opinion of bags.

The chapter on operative obstetrics is well done. The indications and the technic are well given. As a minor point, one may differ with the suggestion that alcohol-acetone-mercurochrome solutions be used in the vagina prior to operation. Because of the irritation and pain if the patient is not anesthetized, most operators prefer a watery solution, as originally suggested by Mayes.

The discussion of puerperal infection is well done. A small error is noted on page 686, the name of Labarraque being incorrectly spelled. The treatment of sepsis is excellent. Another minor point is illustration 1 on page 747. The upper limb in the knee-chest position is too far forward.

The book will be useful to practitioners in the management of their obstetric difficulties. A place exists for it, and it will meet a cordial reception.

**Zahnärztliche Fragen der Kinderheilkunde in der Praxis.** By B. Orban and A. M. Schwarz. Unbound. Price, 3 marks. Pp. 47, with 25 illustrations. Schwarz' presentation deals with the etiology of malocclusion and the means

This publication is comprised of two papers, "The Influence of Nutrition in Children on Tooth Formation," by B. Orban, and "The Interest of the Pediatrician in the Prevention of Irregularities of Tooth Position and of Occlusion," by A. M. Schwarz, reprinted from *Archiv für Kinderheilkunde.*

In the former Orban states that nutrition affects the enamel and dentin of the teeth during their formative period, the most important time being before birth and in early childhood. Defects in calcification are in proportion to the severity and intensity of the insult. The gross and the microscopic imperfection therefore bear a relation to the age of the child at the time of the disturbance. Observation of the areas of the teeth affected suggest the age at which the difficulty occurred. Charts illustrating this relation, based on the tables of Logan and Kronfeld, are among the illustrations.

Schwarz' presentation deals with the etiology of malocclusion and the means of prevention. He states that many defects formerly looked on as abnormal processes are due to the lack of fullest development. The following prophylactic factors are considered important: (1) care that the head is held high and the mouth kept closed in sleep, (2) care that the greatest natural stimulation is afforded when the child takes nourishment, (3) prevention of rickets in small children, (4) care in handling the problem of premature loss or prolonged retention of the milk teeth, (5) breaking sucking habits and (6) supervision by a specialist.

**Children Handicapped by Cerebral Palsy.** By Elizabeth Evans Lord, Ph.D. Cloth. Price, $1.25. Pp. 120, with 9 illustrations. New York: Commonwealth Fund, 1937.

The author is psychologist to the Children's Hospital, Boston. She has studied over 300 children with cerebral palsy. This book is a summary of the impressions gained and a discussion of the problems met in working with these children.

The first chapter was written by Dr. Bronson Crothers. It briefly describes the medical aspects of cerebral palsy. Dr. Crothers states that injury at birth is the most frequent cause. The greater part of the book is devoted to the intelligence responses of the children. The author emphasizes the difficulties encountered in evaluating intelligence, both with and without mental tests, the various types of defects shown and the resulting problems in training and education. A chapter is devoted to the "Teacher Problem," and the final chapter briefly describes some of the emotional problems of the patients and of their parents.

Persons who are working with children with cerebral palsy, who supervise either the medical treatment or the education of these patients or who advise parents about their rearing, will find this book extremely helpful. It is clearly written and interesting and is a contribution to the literature.

# Directory of Pediatric Societies *

## INTERNATIONAL

### International Association of Preventive Pediatrics

President: Professor G. Scheltema, 6a Herreplein, Groningen, Netherlands.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

### International Congress of Pediatrics

President: Prof. Luigi Spolverini, Policlinico Lungo Tevere Melini, 24, Rome, Italy.
Secretary: Professor Vitetti, Rome, Italy.
Place: Rome, Italy. Time: Sept. 27-30, 1937.
American Committee:
Chairman: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary: Dr. L. Emmett Holt Jr., Johns Hopkins Hosp., Baltimore.
Canadian Committee:
Chairman: Dr. H. B. Cushing, 1390 Sherbrooke St., W., Montreal.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St., W., Montreal.

### International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.
Place: Rome, Italy. Time: Oct. 4-8, 1937.

## FOREIGN

### British Paediatric Association

President: Dr. Leonard Findlay, 14 Wimpole St., London, W. 1.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

### Paediatrický Spolok na Slovensku

President: Dr. A. J. Chura, Lazaretská 6, Bratislava, Czechoslovakia.
Secretary: Dr. S. Limbacher, Dlhá 2, Bratislava, Czechoslovakia.
Place: Pediatric Clinic, University, Bratislava. Time: Six times a year.

### Royal Society of Medicine, Section for the Study of Disease in Children

President: Sir Lancelot Barrington-Ward, 85 Harley St., London, W. 1.
Secretary: Dr. K. H. Tallerman, 122 Harley St., London, W. 1.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:30 p. m.

### Palestine Jewish Medical Association, Section of Physicians of Children's Diseases

President: Prof. S. Rosenbaum, 26 Bialikstr., Tel Aviv, Palestine.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv, Palestine.

### Sociedad Cubana de Pediatría

President: Prof. Félix Hurtado Galtés, Carlos III, 7, Havana.
Secretary: Dr. Carlos Hernández Miyares, San Lazaro 370, Havana.
Place: Cátedra de Clínica Infantil, Hospital Mercedes, Havana. Time: Third Thursday of every month.

*Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

## NATIONAL

### American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Clifford D. Sweet, 2940 Summit St., Oakland, Calif.
Secretary: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester, N. Y.
Place: San Francisco. Time: June 13-17, 1938.

### American Academy of Pediatrics

President: Dr. Philip Van Ingen, 125 E. 71st St., New York.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Region I. Place: Boston, Mass. Time: Nov. 12-13, 1937.
Region II. Place: New Orleans, La. Time: Nov. 30-Dec. 1-3, 1937.
Region III. Place: Lake Shore Athletic Club, Chicago. Time: Oct. 14-16, 1937.
Region IV. Place: Los Angeles, Calif. Time: October 1937.

### American Hospital Association, Children's Hospital Section

Chairman: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Secretary: Miss Edith F. Bateman, Shriners' Hospital for Crippled Children, St. Louis, Mo.

### American Pediatric Society

President: Dr. Kenneth D. Blackfan, 300 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.
Place: The Sagamore, Bolton Landing, New York. Time: June 9-11, 1938.

### Canadian Society for the Study of Diseases of Children

President: Dr. Alton Goldbloom, 1543 Crescent St., Montreal, Quebec.
Secretary-Treasurer: Dr. Pearl Summerfeldt, Hospital for Sick Children, Toronto, Ont.

### Society for Pediatric Research

President: Dr. Francis Scott Smyth, University of California Medical School, San Francisco.
Secretary: Dr. A. A. Weech, 3975 Broadway, New York.

## SECTIONAL

### North Pacific Pediatric Society

President: Dr. D. M. Dayton, Medical Arts Bldg., Tacoma, Wash.
Secretary: Dr. H. T. Clay, Medical Arts Bldg., Tacoma, Wash.
Place: Portland, Ore. Time: June 1937.

### Southern Medical Association, Section of Pediatrics

Chairman: Dr. Gilbert Levy, 20 S. Dunlap St., Memphis, Tenn.
Secretary: Dr. Hughes Kennedy Jr., Highland Plaza Apts., Birmingham, Ala.

## STATE

### Alabama Pediatric Society

President: Dr. Wallace A. Clyde, Employees' Hospital, Fairfield.
Secretary-Treasurer: Dr. M. G. Neely, Employees' Hospital, Fairfield.

### Arkansas State Pediatric Association

Chairman: Dr. A. C. Kirby, 701 Main St., Little Rock.
Secretary: Dr. Madeline M. Melson, 909 Main St., Little Rock.

### California State Medical Society, Section on Pediatrics

Chairman: Dr. E. Earl Moody, 3780 Wilshire Blvd., Los Angeles.
Secretary: Dr. Hartzel H. Ray, 23 Second Ave., San Mateo.

### Florida State Pediatric Society

President: Dr. Douglas D. Martin, 442 W. Lafayette St., Tampa.
Secretary: Dr. Warren W. Quillian, 227 Avenue Aragon, Miami.
Place: Concurrent with state association meeting at time of convention.

### Georgia Pediatric Society

President: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St., N. E., Atlanta.

### Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. Howard W. Brayton, 179 Allyn St., Hartford.
Secretary: Dr. Joseph L. Hetzel, 103 N. Main St., Waterbury.

### Indiana State Pediatric Society

President: Dr. Ernest R. Carlo, 2902 Fairfield Ave., Fort Wayne.
Secretary-Treasurer: Dr. Mathew Winters, 23 E. Ohio St., Indianapolis.
Time: Two meetings a year.

### Louisiana State Pediatric Society

President: Dr. Clarence H. Webb, 624 Travis St., Shreveport.
Secretary-Treasurer: Dr. Ruth Aleman, 1407 S. Carrollton Ave., New Orleans.

### Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. George M. Retan, 459 James St., Syracuse.
Secretary: Dr. John D. Craig, 33 E. 61st St., New York.

### Michigan State Medical Society, Pediatric Section

Chairman: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. C. R. Dengler, 131 W. Michigan Ave., Jackson.

### Mississippi State Pediatric Society

President: Dr. Guy C. Jarratt, 920 Cawford St., Vicksburg.
Secretary-Treasurer: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Place: To be designated by Society. Time: Yearly.

### Nebraska Pediatric Society

President: Dr. J. A. Henske, 1614 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. J. H. Murphy, 915 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

### North Carolina Pediatric Society

President: Dr. John LaBruce Ward, Arcade Bldg., Asheville.
Secretary: Dr. Lewis Elias, 36 Grove St., Asheville.

### Oklahoma State Pediatric Society

President: Dr. B. H. Nicholson, 301 N. W. Twelfth St., Oklahoma City.
Secretary: Dr. Hugh C. Graham, 1501 S. Baltimore Ave., Tulsa.

### Pennsylvania Medical Society, Pediatric Section

Chairman: Dr. Theodore O. Elterich, 3700 Fifth Ave., Pittsburgh.
Secretary: Dr. John M. Higgins, Sayre.

### South Carolina Pediatric Society

President: Dr. Leland B. Salters, 317 S. Warley St., Florence.
Secretary-Treasurer: Dr. D. Lesesne Smith Jr., 187 Oakland Ave., Spartanburg.

### Tennessee State Pediatric Society

President: Dr. Joe T. Smith, 702 Medical Arts Bldg., Knoxville.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.

### Texas Pediatric Society

President: Dr. John G. Young, 3930 McKinney Ave., Dallas.
Secretary-Treasurer: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Place: Dallas. Time: Fall.

### Virginia Pediatric Society

President: Dr. Basil B. Jones, 1028 W. Franklin St., Richmond.
Secretary: Dr. W. A. McGee, 616 W. Grace St., Richmond.

### West Virginia State Medical Society, Section on Pediatrics

President: Dr. John T. Thornton, 58 16th St., Wheeling.
Secretary: Dr. Claude L. Holland, 400 Locust Ave., Fairmont.

## LOCAL

### Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. D. Pilcher, City Hosital, Cleveland.
Secretary: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

### Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. T. B. Verner, 170 St. George St., Toronto.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto.

### Bronx Pediatric Society

President: Dr. Daniel J. Doan, 420 E. 159th St., New York.
Secretary: Dr. Samuel T. Levethan, 254 E. 184th St., New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

### Brooklyn Academy of Pediatrics

President: Dr. Walter D. Ludlum, 1421 Cortelyou Rd., Brooklyn.
Secretary: Dr. John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

### Central New York Pediatric Club

President: Dr. Frank Vasder Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

### Chicago Pediatric Society

President: Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.
Secretary: Dr. George F. Munns, 723 Elm St., Winnetka, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave., Chicago. Time: Third Tuesday of each month, October to May, inclusive.

### Dallas Pediatric Society

President: Dr. John Young, 3930 McKinney Ave., Dallas, Texas.
Secretary-Treasurer: Dr. John E. Ashby, 3622 Fairmont Ave., Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

### Detroit Pediatric Society

President: Dr. Edward A. Wishropp, 10 Peterboro St., Detroit.
Secretary: Dr. W. J. Scott, 5140 Second Ave., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

### Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. T. F. Davenport, 104 Ponce de Leon Ave., Atlanta.
Secretary: Dr. James P. Hanner, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

### Houston Pediatric Society

President: Dr. Walter F. Qualtrough, 920 Westheimer Ave., Houston, Texas.
Secretary-Treasurer: Dr. Allan Bloxsom, 4402 Travis St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

### Intermountain Pediatric Society

President: Dr. Eugene Smith, 385 Twenty-Fourth St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

### Kansas City (Missouri) Pediatric Society

President: Dr. W. R. Moore, 620 Francis St., St. Joseph.
Secretary: Dr. F. S. Hogue, 1103 Grand Ave., Kansas City.
Place: Kansas City General Hospital. Time: On call.

### Los Angeles County Medical Association, Pediatric Section

President: Dr. Edwin F. Patton, 3875 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Henry F. Gallagher, 1930 Wilshire Blvd., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd.
Time: Second Monday of February, April, June, October and December.

### Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Harry R. Litchfield, 163 Eastern Parkway, Brooklyn.
Secretary: Dr. Jacob Rosenblum, 550 Ocean Ave., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: Third Wednesday of each month, October to May.

### Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. W. C. A. Steffen, 42 Union St., Flushing, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144 38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

### Memphis Pediatric Society

President: Dr. Clyde V. Croswell, 1052 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. David W. Goltman, 1073 Madison Ave., Memphis, Tenn
Place: John Gaston Hospital. Time: Quarterly.

### Milwaukee Pediatric Society

President: Dr. George F. Kelly, 425 E. Wisconsin St., Milwaukee.
Secretary: Dr. Helen Jane Zilmer, 781 N. Jefferson St., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

### New England Pediatric Society

President: Dr. Henry E. Utter, 122 Waterman St., Providence, R. I.
Secretary-Treasurer: Dr. Henry E. Gallup, 1101 Beacon St., Brookline, Mass.
Place: Boston Medical Library. Time: Four meeting a year, occurring from September to May.

### New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Alexander T. Martin, 107 E. 85th St., New York.
Secretary: Dr. Philip M. Stimson, 25 Claremont Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

### Northwestern Pediatric Society

President: Dr. A. V. Stoesser, University Hospital, Minneapolis.
Secretary: Dr. Roger L. J. Kennedy, Mayo Clinic, Rochester, Minn.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

### Oklahoma City Pediatric Society

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 1200 N. Walker St., Oklahoma City.
Time: Alternate months.

### Philadelphia Pediatric Society

President: Dr. Emily Bacon, 2104 Spruce St., Philadelphia.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

### Pittsburgh Pediatric Society

President: Dr. James LeRoy Foster, Highland Bldg., Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200 Fifth Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

### Richmond Pediatric Society

President: Dr. Lee E. Sutton Jr., 2601 Grove Ave., Richmond, Va.
Secretary-Treasurer: Dr. Louise Fry Galvin, 2416 Stuart Ave., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

### Rochester Pediatric Society

President: Dr. F. W. Bush, 29 N. Goodman St., Rochester, N. Y.
Secretary: Dr. David Wolin, 16 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

### Rocky Mountain Pediatric Society

President: Dr. James E. Russell Jr., 820 Metropolitan Bldg., Denver.
Secretary: Dr. F. Craig Johnson, 1850 Gilpin St., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 2:30 p. m.

### St. Louis Pediatric Society

President: Dr. John Zahorsky, 536 N. Taylor Ave., St. Louis.
Secretary-Treasurer: Dr. Max Deutch, 634 N. Grand Blvd., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Frank H. Douglass, Medical Dental Bldg., Seattle.
Secretary: Dr. C. Lu Verne Smith, Stimson Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Howard R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Secretary: Dr. Philip E. Rothman, 3875 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. M. Cooperstock, Northern Michigan Children's Clinic, Marquette.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.

WESTCHESTER COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION (NEW YORK)

President: Dr. Louis V. Waldron, 149 N. Broadway, Yonkers, N. Y.
Secretary-Treasurer: Dr. Fairfax Hall, 421 Huguenot St., New Rochelle, N. Y.
Place: Grasslands Hospital. Time: Third Thursday, October, December, February and April.